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TROPICAL DISEASES

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PARASITE OF KALA-AZAR.

1, free forms from the spleen; 2 and 3, in the endothelial cells; 4, in the liver.

PARASITE OF ORIENTAL SORE.

5, in endothelial cell; 6, free forms.

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TROPICAL DISEASES

A MANUAL OF THE DISEASES OF WARM CLIMATES

BY

SIR PATRICK MANSON

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WITH SEVEN COLOURED PLATES

AND 241 PLAIN FIGURES

FOURTH EDITION, THOROUGHLY REVISED AND ENLARGED

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PREFACE TO FOURTH EDITION

SINCE the publication of the first edition of this manual, in 1898, tropical medicine has undergone a remarkable development. Schools of Tropical Medicine, recently established in this country, in Germany, and in France, have sent out a large number of men thoroughly trained not only in tropical practice, but also in lines of investigation specially calculated to advance the subject. Our own Government and those of India, America, Germany, and Portugal, besides the Royal Society and several of the Tropical Schools, have from time to time despatched Commissions to clear up particular points in tropical disease. The British, the Indian, and many of the Colonial Governments have not only given pecuniary help to the Tropical Schools, but have established special laboratories in suitable places, and in these and other ways have subsidised research in tropical medicine. The British Medical Association has instituted a Tropical Section at its annual meetings, and the Journal of the Association, and other leading medical journals, have thrown open their columns more liberally than heretofore to contributors in this branch of medicine. The general public also has shown unusual interest in several recent discoveries, and both directly and indirectly has done not a little to support and encourage the profession in its endeavours to advance tropical medicine.

The result of all this has been a phenomenal activity in the study of tropical disease and a corresponding advance in knowledge.

It would be impossible to indicate here all that has been accomplished during these last nine years, but I might point more especially to the definite installation of the mosquito as a leading factor in tropical pathology; the establishment of the mosquito-malaria

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theory; the discovery of the relationship of this insect to yellow fever; the discovery of the precise way in which *Filaria bancrofti* is inoculated by the mosquito; the discovery of a trypanosome in man, and its relation to sleeping sickness; the discovery of an unsuspected route by which *Ankylostomum duodenale* gets access to the human intestine; the discovery of the nature and germ of kala-azar and tropical sore; the discovery of a new form of relapsing fever and of its transmitting agent; the definite establishment of the rat flea as the communicator of plague. Furthermore, these discoveries in tropical pathology, besides introducing new and probably fertile ideas into general pathology, have led to the elucidation of a number of allied diseases of the lower animals, and have thus an economic as well as a scientific value. Several new diseases have been added to the category of tropical ailments, and, although I cannot chronicle many important therapeutical advances, much has been added to our knowledge of preventive medicine and considerable additions have been made to our means of diagnosis.

These and other important discoveries and developments have entailed extensive revision of this manual, and many additions to the number of its illustrations. For most of the latter I am indebted to the skilful pencil of Mr. A. E. Terzi. Among the sources from which illustrations have been drawn I would mention Professor Looss's contribution to Mense's "Handbuch der Tropenkrankheiten." I desire especially to acknowledge my obligation to Dr. L. Sambon for much assistance in bringing the zoological information and nomenclature up to date. Although every endeavour has been made to confine the book to its original modest dimensions, I regret to find that a material addition to its size has been inevitable. Notwithstanding this, I trust the manual may still be found to fulfil its original purpose of conveying adequate information in reasonably small compass.

P. M.

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PREFACE TO FIRST EDITION

A MANUAL on the diseases of warm climates, of handy size, and yet giving adequate information, has long been a want; for the exigencies of travel and of tropical life are, as a rule, incompatible with big volumes and large libraries. This is the reason for the present work.

While it is hoped that the book may prove of practical service, it makes no pretension to being anything more than an introduction to the important department of medicine of which it treats; in no sense is it put forward as a complete treatise, or as being in this respect comparable to the more elaborate works by Davidson, Scheube, Rho, Laveran, Corre, Roux, and other systematic writers in the same field.

The author avails himself of this opportunity to acknowledge the valuable assistance he has received, in revising the text, from Dr. L. Westenra Sambon and Mr. David Rees, M.R.C.P., L.R.C.P., Superintendent, London School of Tropical Medicine. He would also acknowledge his great obligation to Mr. Richard Muir, Pathological Laboratory, Edinburgh University, for his care and skill in preparing the illustrations.

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INTRODUCTION

THE ÆTIOLOGY OF TROPICAL DISEASES

THE title which I have elected to give to this work, TROPICAL DISEASES, is more convenient than accurate. If by "tropical diseases" be meant diseases peculiar to the tropics, then half a dozen pages might have sufficed for their description; for, at most, only two or three comparatively unimportant diseases strictly deserve that title. If, on the other hand, the expression "tropical diseases" be held to include all diseases occurring in the tropics, then the work would require to cover almost the entire range of medicine; for the diseases of temperate climates are also, and in almost every instance, to be found in tropical climates.

I employ the term "tropical" in a meteorological, rather than in a geographical, sense, meaning by it sustained high atmospheric temperature; and by the term "tropical diseases" I wish to indicate diseases occurring only, or which from one circumstance or another are specially prevalent, in warm climates.

It must not be inferred from this, however, that high atmospheric temperature is the sole and direct cause of the bulk of tropical diseases. The physiological machinery of the human body is so adjusted that great variations of atmospheric temperature can be supported by man with impunity. Indeed, although temperature acts as an important pathogenic factor, it is very rarely that it does so directly. Extreme cold may cause frost-bite; exposure to the sun, sun erythema, sun headache, and symptomatic fever; a hot atmosphere, heat exhaustion; prolonged residence in hot moist climates, vague, ill-defined conditions of debility; profuse sweating from heat of climate,

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prickly heat. But none of these states can with justice be regarded as disease.

This being so, it is natural to ask: In what way do tropical influences affect disease, as they undoubtedly do; and why should it be that some diseases are peculiar to tropical climates, or are specially prevalent in such climates?

Speaking generally, the natives of tropical countries are not injuriously affected by the meteorological conditions of the climates they live in, any more than are the inhabitants of more temperate climates; their physiological activities are attuned by heredity and habit to the conditions they were born into. The European, it may be, on his first entering the tropics, and until his machinery has adjusted itself to the altered meteorological circumstances, is liable to slight physiological irregularities, and this more especially if he persist in the dietetic habits appropriate to his native land. A predisposition to certain diseases, and a tendency to degenerative changes, may be brought about in this way; but acute disease, with active tissue change, is not so caused. In the tropics, as in temperate climates, in the European and in the native alike, nearly all disease is of specific origin. It is in their specific causes that the difference between the diseases of temperate climates and those of tropical climates principally lies.

Modern science has clearly shown that nearly all diseases, directly or indirectly, are caused by germs. It must be confessed that although in many instances these germs have been discovered, in other instances they are yet to find; nevertheless, their existence in the latter may be confidently postulated.

Germs are living organisms, and, like all living things, demand certain physical conditions for their well-being. One of these conditions is a certain temperature; another is certain media; and a third is certain opportunities.

In the majority of instances disease germs are true parasites, and therefore, to keep in existence as species, require to pass from host to host. If, during this passage from host to host, the temperature of the

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transmitting medium—be it air, water, or food—be too high or too low for the special requirements of the germ in question, that germ dies and ceases to be infective. In this way may be explained the absence from the tropics of a class of directly infectious diseases represented by scarlet fever, and the absence from temperate climates of a similar class of diseases represented perhaps by dengue. In the one case, during the short passage from one human being to another, tropical temperature is fatal to the air-borne germ; in the other it may be that the lower temperature of higher latitudes has the same effect.

In another type of disease, of which tropical scaly ringworm (tinea imbricata) is an excellent example, the germ vegetates on the surface of the body, and is thus exposed to the vicissitudes of climate. One of the requirements of the germ referred to is a high atmospheric temperature and a certain degree of moisture. Given these it flourishes; remove these and it dies out, just as a palm tree or a bird of paradise would die on being transferred to a cold climate.

Many diseases require for their transmission from one individual to another the services of a third and wholly different animal. The propagation and continued existence of a disease of this description will depend, therefore, on the presence of the third animal. If the latter be a tropical species, the disease for the transmission of which it is indispensable must necessarily be confined to the tropics. Thus the geographical range of malaria and of filariasis is determined by that of certain species of mosquito which ingest and act as alternative hosts to the respective germs, and, so to speak, prepare them for entrance into their human host. The distribution of a large number of animal parasitic diseases depends in this way on the distribution of these alternative hosts. When this animal happens to be a tropical species, the disease it subtends, so to speak, is, in natural conditions, necessarily tropical also.

Certain diseases are common to man and the lower animals. If these latter happen to be tropical species

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the opportunities for man to contract the common disease are most frequent, or are only found, in the tropics. Such, most probably, are some of the tropical ringworms.

Certain parasites are so organised that before re-entering man they must pass a part of their lives as free organisms in the outer world, where they require a relatively high temperature for their development. Such parasites, therefore, and the diseases they give rise to, must necessarily be tropical or sub-tropical. The *Ankylostomum duodenale* and ankylostomiasis are an instance in point.

There is a class of intoxication diseases which depend on toxins generated by germs whose habitat is the soil, water, or other external media, and whose germs do not enter the human body as a necessary feature in their life histories, although their toxins may. The yeast plant and its toxin, alcohol, and the disease it causes, alcoholism, are the most familiar example of this. Such, too, are ergotism, atriplicism, and, perhaps, lathyrism. The beriberi germ, its toxin, and beriberi, are possibly another. These germs require certain temperatures and certain media; consequently the diseases they produce have a corresponding geographical range. If one of these conditions be a high temperature, the disease, as in the case of beriberi, is mainly a tropical one.

Lastly, I can conceive, and believe, that there is another and less directly-acting set of conditions influencing the distribution of disease, conditions which as yet have been ignored by epidemiologists, but which, it seems to me, must have an important bearing on this subject. Disease germs, their transmitting agencies, or their intermediate hosts, being living organisms, are, during their extracorporeal phases, necessarily competing organisms, and therefore liable to be preyed upon or otherwise crushed out by other organisms in the struggle for existence. The malaria parasite is absent in many places in which, apparently, all the conditions favourable to its existence are to be found in perfection. Why is it not found there, seeing that it must certainly have been fre-

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quently introduced? I would suggest that in some instances this and other disease germs, or the organisms subtending them, are kept under by natural enemies which prey on them, just as fishes prey on and keep down water-haunting insects, or as mice do humble-bees. The geographical range of such disease germs, therefore, will depend, not only on the presence of favourable conditions, but, also, on the absence of unfavourable ones. Herein lies a vast field for study, and one which, as yet, has not been touched by epidemiologists.

In these and similar ways the peculiar distribution of tropical diseases is regulated. The more we learn about these diseases the less important in its bearing on their geographical distribution, and as a direct pathogenic agency, becomes the *rôle* of temperature *per se*, and the more important the influence of the tropical fauna.

Whatever may have been the original source of the pathogenic parasites of man, it is certain that many of those which have a wide distribution at the present day were much more restricted originally. The extension of many of them has occurred within historical, and of some even in recent times. Thus, in the last century, cholera spread over a great part of the world from its reputed home in India. Small-pox and other Old-World diseases have crossed the Atlantic; and some originally American diseases, such as syphilis and the jigger, have appeared in the Old World; measles, whooping-cough, tuberculosis, and leprosy have been introduced into the Pacific Islands. The process of diffusion is still proceeding, assisted, doubtless, by the vastly increased rapidity and frequency of modern travel, and by the breaking down in recent times of social, political, and physical barriers which formerly isolated many communities, some of which had been from time immemorial the sole repositories of particular disease germs. Thus the sleeping sickness of West Africa is passing to East Africa, and thus, most probably, the yellow fever of America will pass to Asia.

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There is one factor which undoubtedly has contributed powerfully to delay the diffusion of certain tropical diseases — the circumstance that most of them depend on protozoal or some other kind of animal germ requiring for its transmission an animal intermediary. Diseases which depend on bacterial germs, if their special bacterium be introduced, social and sanitary conditions being favourable, will spread in any country or climate, and thus it is that all bacterial diseases, with hardly an exception, are found, or are capable of existing, everywhere; in the passage from host to host their germs are not killed by ordinary atmospheric conditions, and they require no second intermediary. Diseases depending on protozoa or other animal germs, in many though not in all instances, will not establish themselves thus universally, because their germs in the passage from host to host demand, through their intermediaries or otherwise, very special and climatically restricted conditions. Tropical diseases belong for the most part to this category, and therefore their successful introduction and spread to new ground are attended with more difficulty than bacterial diseases, demanding, as the former generally do, the double condition of the introduction not only of the germ itself, but also of the intermediary.

Although this double necessity has undoubtedly operated powerfully against the spread of certain tropical diseases, there is reason to believe that in time this difficulty will disappear; for, so far as we know, there is no reason why, if introduced into new places, these animal intermediaries should not obtain a permanent footing and spread.

There are many instances of exotic insects, for example, which have established themselves after either accidental or intentional introduction into new countries. There is no reason, therefore, for thinking that disease-germ insect intermediaries could not be similarly established in countries in which they are unknown at present. Thus, if the tse-tse flies were successfully introduced into India, sleeping sickness might appear there in due course;

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or, if appropriate anopheles were introduced into many at present malaria-free and salubrious Pacific Islands, malaria would become established there. And, thus, though certain tropical diseases have at present a limited range, there is great probability, unless measures are speedily set on foot to prevent such a calamity, that the swift and increasing intercourse of modern times, by facilitating the intentional or accidental introduction of their subserving intermediaries, will ere long enable them to extend their present geographical range.

It is evident from what has been advanced that the student of medicine must be a naturalist before he can hope to become a scientific epidemiologist, or pathologist, or a capable practitioner. The necessity for this in all departments of medicine is yearly becoming more apparent, but especially so in that section of medicine which relates to tropical disease. This is further accentuated if we reflect that, although we do know something about a few of the tropical diseases and their germs, there must be many more tropical diseases and tropical disease germs about which we know absolutely nothing. Who can doubt that just as the fauna and flora of the tropical world are infinitely richer in species than those of colder climates, so there is a corresponding distribution in the wealth and poverty of pathogenic organisms; and that many, if not most, of the tropical diseases have yet to be differentiated? The discoveries of the last few years show this. Opportunities and appliances for original pathological study are, from circumstances, too often wanting to the tropical practitioner; but in this matter of the ætiology of disease he certainly enjoys opportunities for original research and discovery far superior in novelty and interest to those at the command of his fellow inquirer in the well-worked field of European and American research.

In the following pages I have included certain cosmopolitan diseases, such as leprosy and plague, diseases which, properly speaking, do not depend in any very special way, or necessarily, on climatic conditions. They have been practically ousted from

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Europe and the temperate parts of America by the spread of civilisation and the improved hygiene that has followed in its train. They are now virtually confined to tropical and sub-tropical countries, where they still survive under those backward social and sanitary conditions which are necessary for their successful propagation, and which are more or less an indirect outcome of tropical climate.

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TROPICAL DISEASES

SECTION I.—FEVERS

CHAPTER I

MALARIA

Definition.—Morbid conditions produced by certain protozoal parasites belonging to the Class *Sporozoa*, whose definitive host is the mosquito, and whose intermediate host is man and, possibly, other vertebrates. In man these parasites inhabit the red blood corpuscles, giving rise to fever—usually of a periodic character, anæmia, enlargement of the spleen, and the deposit of a black pigment in the viscera and elsewhere. Some of their phases are amenable to quinine.

HISTORY

The history of malaria goes back to times of remotest antiquity. Already in the fifth century B.C. Hippocrates recognised the existence of periodic fevers, and divided them into quotidian, tertian, sub-tertian and quartan. Galen, Celsus, and other Roman writers also gave accurate descriptions of these fevers.

From the classic period until about the middle of the seventeenth century there was no material advance in knowledge regarding malaria, but the introduction of cinchona in 1640 enabled Morton and Tort to separate the malarial fevers from other febrile diseases, and to show that some continued and remitting fevers belong to the same group as the intermittents.

The next important step was the discovery of the characteristic pigmentation of the viscera in malaria. In 1847, Meckel described certain pigment-bearing

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cells which he had found in the spleen and in the blood at the *post-mortem* of a patient who had died of malaria. Virchow was able to confirm this observation, and Planer in 1854 noted these pigmented cells in fresh blood from the finger of malarial patients. These cells were, of course, the malarial parasites, although their true nature was not apprehended at the time.

The parasitic nature of malaria, which had been suspected since the days of Varro and Columella, was definitely established by Laveran, who in 1880, having noticed the eruption of long motile filaments from the pigmented cells described by Meckel and Planer, was the first to recognise their parasitic character.

Laveran's observations were soon extended by Marchiafava, Celli, Golgi, Bignami, Bastianelli, and other investigators, but especially by Golgi, who demonstrated the definite correlation between the development of the parasites and the periodicity of the fever paroxysms, and showed that the different types of malarial fever correspond to different species of parasites.

The association of the malarial parasites with certain mosquitoes, suggested by epidemiological facts, and by certain phases in the life history of the parasite indicating the necessity of alternation of generations, together with a change of host as in other hæmo-parasites, was definitely established by Ross's investigations and the experiments carried out by the Italians and ourselves.

Finally the application of these recent discoveries to the diagnosis and prevention of malaria has led to practical measures which have already been fruitful in good results and promise yet more.

ÆTIOLOGY

Proofs that the malaria parasites are the cause of malarial disease.—It is now certain that the presence and proliferation in the blood of these parasites, discovered by Laveran in 1880, are the cause of what was formerly and is still known as "malarial disease." The following are the principal reasons for this belief:—

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1. The occurrence of the parasites in the blood is practically always, sooner or later, associated with the clinical phenomena of malarial infection.

2. Malarial fever throughout, or at one time or another during its course, is invariably associated with the presence of one or other of these parasites in the blood.

3. The phases of a malarial fever bear a definite relation to the phases of the life-cycle of the particular parasites present in the blood.

4. That absolutely characteristic feature of malarial disease—malarial pigmentation of viscera—is fully accounted for by the pigment-forming property of the parasites.

5. Intravenous or subcutaneous injection of blood from a case of malarial infection—that is, of blood containing the parasite—is generally, after an incubation period of eight to twelve days, followed by an attack of malarial fever, and by the appearance in the blood of the person injected of the same species of malaria parasite.

6. The administration of quinine, which brings about the cessation of the clinical symptoms of acute malarial infection, rapidly causes most phases of the parasite to disappear from the blood.

7. If, after they have imbibed malarial blood, certain species of mosquitoes be dissected at serial intervals, the evolution of the malaria parasite can be followed in their tissues until, finally, the germs of the parasite can be tracked into the cells and secretion of the salivary glands of the insect.

8. If after a week, or thereabouts, a similarly-fed mosquito bite a hitherto uninfected man, in many instances, after a few days, that man will exhibit the clinical phenomena of malarial infection and the characteristic parasite in his blood.

9. A non-immune, if effectually protected against mosquito bite, will not contract malarial disease however long he may live in highly malarious localities.

The proof of the causal relationship of the parasite to the disease may therefore be said to be complete.

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MORPHOLOGY AND HISTOLOGY

There are several species of malaria parasites. The distinctive characteristics of each of these will be detailed in Chapter III. The following brief description is confined to what may be regarded as the generic features common to all.

The three phases.—The malaria parasite, like all true parasites, must be adapted not only for a life inside its hosts, but also, in order that its continuance as a species may be assured, for a passage from one host to another. Consequently, as regards man, it exhibits two distinct phases—an intracorporeal and an extracorporeal. Clinical observation

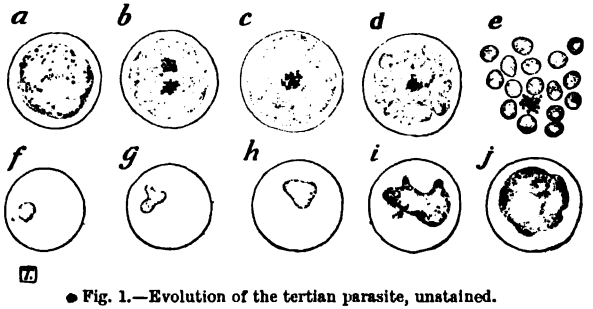

Fig. 1.—Evolution of the tertian parasite, unstained.

and analogy make it certain that there is yet another phase, also intracorporeal—the latent phase, whose characters as yet can only be conjectured.

INTRACORPOREAL OR HUMAN CYCLE

Each species of malaria parasite has its special and more or less definite intracorporeal life-span or cycle of twenty-four hours, of forty-eight hours, or of seventy-two hours.

On examining microscopically malarial blood towards the end of one of these cycles, an hour or two before the occurrence of a paroxysm of the characteristic periodic fever it induces, the parasite may be recognised as a pale, somewhat ill-defined disc of protoplasm occupying a larger or smaller area within

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a proportion of the red blood corpuscles (Fig. 1, *a*). Scattered through this pale body are a number of intensely black or reddish-black particles—an excrementitious material called hæmozoin.*

Changes in the parasite.—By making fresh blood preparations and repeating his examinations at short serial intervals, the observer is enabled to infer that the following changes systematically occur in this disc of pigmented protoplasm. After a time, as the parasite matures, the scattered hæmozoin particles collect into little groups, sometimes into radiating lines. These hæmozoin groups subsequently concentrate into one or two larger and more or less central blocks, around which the pale protoplasm of the parasite arranges itself in minute segments which finally acquire a globular form and appear as well-defined spherules (Fig. 1, *b*, *c*, *d*). The including blood corpuscle then breaks down and the spherules, none of which contains hæmozoin, fall apart, and, along with the clump or clumps of hæmozoin, become free in the liquor sanguinis (Fig. 1, *e*). The phagocytes now quickly absorb the hæmozoin and many of the spherules. A proportion of the latter, escaping the phagocytes, attach themselves to other blood corpuscles which they contrive to enter (Fig. 1, *f*). In the interior of these newly infected corpuscles the young parasites exhibit active amœboid movement, shooting out and retracting long pseudopodia, and growing at the expense of the hæmoglobin (Fig. 1, *g*). This substance they assimilate, converting it into the pale protoplasmic material constituting the mass of the parasite and into the hæmozoin particles (Fig. 1, *h*, *i*). As the parasite becomes larger its amœboid movements gradually slow down until all motion finally ceases; just before the formation of spherules and completion of the cycle (Fig. 1, *j*), beyond slight translation movement of the hæmozoin particles, the parasite is passive.

* The term "hæmozoin" suggested by Sambon is here employed instead of "melanin" hitherto in use, which has a definite and different physiological meaning. The term "black pigment" is vague and incorrect.

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Structure of the parasite.—By appropriate staining of the free spherule (Fig. 2, *b*, *c*, *d*) it is found to consist of a minute, deeply tinted chromatin mass the nucleolus, surrounded by an unstained area regarded by many as a vesicular nucleus, and this again by a somewhat lightly tinted covering of protoplasm. After the spherule has entered a blood corpuscle (Fig. 2, *e*), staining shows that the vesicular nucleus has become larger and more distinct, that the protoplasm has increased in bulk, and that the deeply stained nucleolus, which is sometimes double, has come to lie eccentrically in the nucleus, and both of them eccentrically in the protoplasm. On account of the relatively large size of the unstained nucleus, the

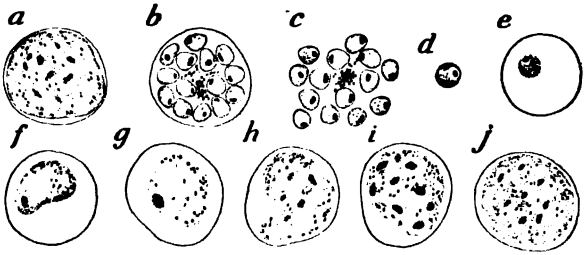

Fig. 2.—Evolution of the tertian parasite, stained.

eccentric position of the deeply stained nucleolus, and the narrow rim of stained protoplasm, the younger parasites look like so many minute blue signet-rings stuck on to the blood corpuscles. As the parasite grows and approaches maturity the nucleolus enlarges, becomes less defined, and then disperses; the vesicular nucleus also becomes enlarged and less distinct (Fig. 2, *f*, *g*, *h*, *i*). Finally, just before sporulation, both nucleus and nucleolus cease to be distinguishable (Fig. 2, *j*, *a*). At this stage these elements become fragmented and diffused throughout the protoplasm. Later the nuclear elements reappear as numerous minute, scattered nucleoli; and it is around these that the protoplasm of the segmenting parasite arranges itself to form the spherules

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(Fig. 2, *b*, *c*). The vesicular character of the nucleus does not usually appear in the spherules until after these have become free in the liquor sanguinis (Fig. 2, *d*).

The hæmozoin particles, so characteristic of the malaria germ, occur as black or very dark red dust-like specks, coarse grains, or short rods, either isolated or aggregated into larger or smaller, more or less dense clumps. Until the concentration of hæmozoin which precedes the formation of spherules takes place the particles are scattered, being located principally in the outer zone, or ectosarc, of the parasite. Apparently so long as the nucleus remains entire the hæmozoin is peripheral; when segmentation occurs in the nucleus the hæmozoin becomes central.

Such is a brief account of the cycle and structure of one phase of the parasite. From it we may understand how the parasite maintains itself and multiplies inside the human body. It does not explain, however, the two other important biological features which analogy and observation clearly indicate—namely, its latency in, and its life outside, the human body.

Latent phase.—It is a well-established fact that, concurrently with the subsidence of acute clinical symptoms, the malaria parasite may disappear from the general circulation. This it does either spontaneously or as a result of the administration of quinine. In the majority of instances the disappearance is only temporary. Usually, after an interval of weeks or months, the parasite reappears in the general circulation and there is a renewal of the clinical phenomena. As to the organ or tissue it selects, or as to its appearance and structure during this time of latency, or as to the exact conditions which cause it once more to resume active, propagating, circulating life, nothing is positively known. This much, however, we do know—namely, that physiological strain or vital depression in the host tends to bring about conditions which break up, and that quinine and vital vigour tend to bring about conditions which favour, latency.

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EXTRACORPOREAL OR MOSQUITO CYCLE

As it is unreasonable to suppose that an organism which propagates so actively in the human body has no opportunity, either by passing from one host to another or in other ways, of continuing its species, we are forced to conclude that some provision must exist in the economy of the parasite that enables it to leave and enter successive hosts. The problems suggested by this consideration are: First, how does the malaria parasite leave the human body;

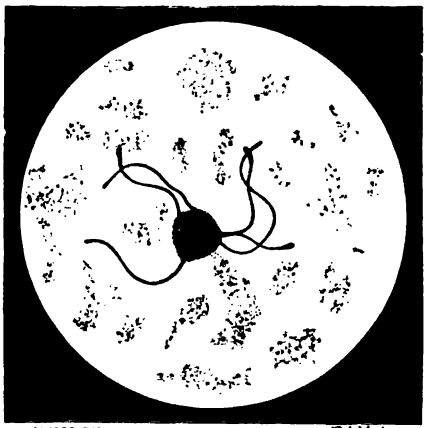

Fig. 3.—Malaria parasite: flagellated body, stained.

second, what is its life when temporarily outside the human body; and, third, how does the parasite re-enter the human body?

The flagellated body.—When fresh malarial blood is examined some time after it has been mounted as a wet preparation, it is no unusual thing to see what is known as the "flagellated body"* (Fig. 3).

* The expressions "flagellated body" and "flagellum," applied to this phase of the malaria parasite, though graphic enough, are somewhat misleading. The flagella of the malaria parasite are in no sense analogous to the flagella of the flagellata; they really function as spermatozoa. The proper zoological terms for this and the other phases of the malaria parasites are given at page 128.

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Analogous bodies are found in all forms of malaria, both in those special to man and in the corresponding infections of the other vertebrata. It is a strange-looking, octopus-like creature with long, actively-moving arms. Though composed of the same materials—namely, colourless protoplasm and dark hæmozoin granules—it differs in many respects from the ordinary forms of the parasite, more especially in the fact that it is not intracorpuscular, but free in the liquor sanguinis. The long, whip-like arms,

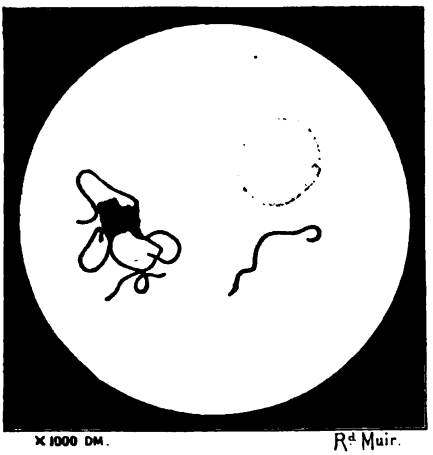

Fig. 4.—Malaria parasite: flagellated body and free swimming microgamete.

numbering from one to six, or even more, are usually designated *flagella* or, more correctly, microgametes. These are exceedingly delicate and pliant filaments, difficult to see not only on account of their delicacy but also on account of the rapidity of their movements. Sometimes bulbous at the free extremity, sometimes presenting one or more swellings in their continuity, the microgametes are three or four times as long as a blood corpuscle is broad. At first they are attached to the periphery of the pigmented central, more or less spherical body, which is about

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half the diameter of a red blood corpuscle. Their movements are so vigorous that they double up or otherwise distort temporarily those corpuscles with which they chance to come in contact. Occasionally it may be observed that one or more of the microgametes break away from the central sphere and swim free in the blood (Fig. 4), remaining active for a considerable time—several hours perhaps—before finally vanishing. When swimming free in the plasma, and also while still attached to the sphere, the microgamete indulges in three kinds of movement:—(*a*) an undulatory movement, evidently subserving locomotion; (*b*) a vibratory movement, apparently provoked by contact with a resisting body, as a blood corpuscle, for in such circumstances the little filament is sometimes seen to straighten itself out and quiver like a slender rod when it is struck on the ground; (*c*) a coiling up movement, usually seen just before the microgamete finally ceases to move.

It is of importance to bear in mind that these flagellated bodies are never seen in newly drawn blood, and that they come into view only after the slide has been mounted for some time—ten to thirty minutes, or even longer, according to circumstances.

Source of the flagellated body.—Careful observation shows that the flagellated bodies are developed from a particular phase of the intracorpuscular parasite, a phase which differs in form according to species—namely, in certain types from what is known as the "crescent body"; in other types from certain large intracorpuscular parasites closely resembling the mature parasite (Fig 1, *j*) just prior to concentration of hæmozoin and segmentation.

The crescent body.—These bodies, and consequently the flagellated body, are not present in the blood at the commencement of a malarial infection, or necessarily, especially if it be long delayed, at the commencement of the recrudescence of a latent infection. They come into the blood only after a week or ten days of acute clinical symptoms. At first few in number, and perhaps difficult to find, they gradually become more numerous, persist for days after the

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disappearance of the other forms of the parasite and the decline of the acute symptoms, and then gradually disappear. Unlike the other forms of the parasite, they are not affected by quinine. They may vanish from the blood after a week, or persist in it for six weeks or longer. They may be very numerous, several in every field of the microscope, or so scanty that many preparations may have to be searched before one is found. Not infrequently they cannot be discovered at all; especially is this the case in

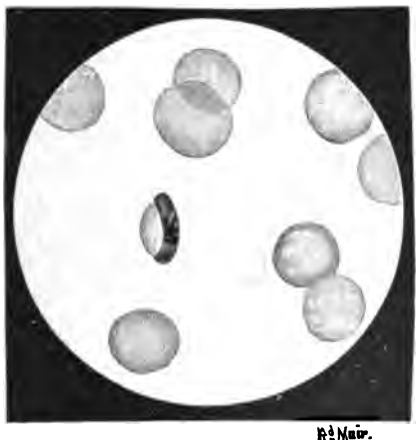

Fig. 5.—Malaria parasite: the crescent body; stained. (× 1000.)

malignant (subtertian) infections in the tropics, although, strange to say, when the same patients suffer a relapse in Europe it is generally easy enough to find the crescent body in the blood.

The shape, size, and structure of the crescent body can best be comprehended from the illustration (Fig. 5). It exhibits no amœboid movements. The principal features to be noted are its very definite crescentic shape; the probable existence of a delicate limiting membrane; the presence of needle-shaped hæmozoin particles, usually about the

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centre of the parasite, though sometimes nearer one end; and a bow-like and exceedingly delicate line that, springing from a point somewhat inside the rounded-off tips of the horns of the crescent, bridges its concavity. Manifestly this bow represents the outline of the remains of the blood corpuscle in which the parasite had developed. In many instances, especially in stained specimens, the continuation of the red blood corpuscle can be distinctly traced around the convexity of the crescent. This circumstance, together with the fact that the material included by the bow and also occasionally seen as a delicate, sometimes slightly jagged fringe around the convexity of the crescent, gives the staining reactions of hæmoglobin, proves that this form of the malaria parasite, like the ordinary amœboid bodies already described, is also intracorpuscular. Slight differences, particularly as regards the sharpness or obtuseness of the horns, occur; but, on the whole, the crescents are very uniform in appearance. Very rarely twin or double crescents—that is, two crescents in one corpuscle—are encountered (Fig. 6).

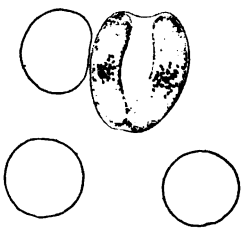

Fig. 6.—Malaria parasite: twin crescents.

Crescents differ in appearance according to their age; in some the hæmozoin granules are scattered throughout the parasite, in others they are concentrated, and in a third class the protoplasm shows vacuolation and other signs of degeneration. The first, it is believed, are young and immature, the second mature, and the third effete parasites. In the first, the hæmozoin rods sometimes exhibit slight translation as well as vibratory movements; in the two latter the hæmozoin is quiescent. The first, or younger, type of crescent stains uniformly; but in the second type the staining, in many instances, is markedly bipolar, a clear, unstained area occupying the middle of each horn, whilst a zone of stained protoplasm forms the

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periphery, and a bridge of stained material divides the two horns at the centre of the crescent. By dissolving the hæmozoin particles at the centre of the crescent with weak solution of ammonia, and subsequently staining, a nucleolus, sometimes double, can be demonstrated.

As will be shown in the sequel, these crescent bodies and the large intracorpuscular forms just alluded to are sexual in their functions. As regards the crescents, there are certain differences in the appearance of the protoplasm, in the arrangement of the pigment, and in the characters of the nucleus as revealed by staining which are distinctive of the male and female crescents respectively. In one type of crescent the protoplasm is hyaline and the hæmozoin somewhat loosely arranged. In another type the protoplasm is faintly granular and the hæmozoin more concentrated, being arranged as a well-defined ring about the centre of the parasite. The former is male, the latter female. The protoplasm of the male parasite stains more deeply, and its nucleus is larger than that of the female parasite.

The more immature forms of the crescent are said to begin to be recognisable in the spleen and bone marrow about the fourth day after a subtertian malarial attack commences. At first, according to Bastianelli and Bignami, they are minute, highly refringent amœboid bodies. They are rarely encountered in peripheral blood; there the crescent body does not begin to show itself till it approaches maturity, about a week after the first crop of amœboid parasites associated with the fever paroxysm has appeared.

Formation of the flagellated body.—Ordinarily, if a number of crescent bodies are kept for a time under observation on the microscope slide, a certain proportion of them will be seen slowly, or more rapidly, to undergo change of shape, gradually becoming converted into squat crescents, then into oval bodies, and then into spheres (Fig. 7, *a*, *b*, *c*), whilst the remains of the enclosing blood corpuscle fall to pieces or melt away. The remains of the blood corpuscle are often seen as a small, slightly

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hæmoglobin-tinted globule lying in contact with or near the parasite. The crescent-derived spheres are of two types in correspondence with the sex of the particular crescent from which they originate, some—the male—having hyaline, others—the female—having granular, protoplasm. At first the hæmozoin particles in the crescent, in the oval body, and in the sphere are motionless and central; more rarely they are eccentric. By and by, in many of the spheres these particles tend to arrange themselves as a ring, lying in contact with the inner surface of what may be a very fine, invisible membrane, occupying the central third of the sphere, and forming, as it

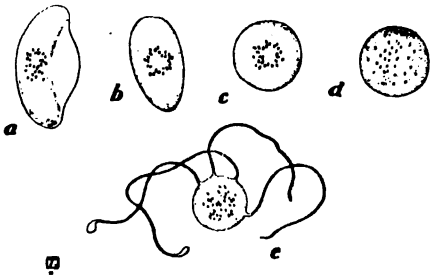

Fig. 7.—Evolution of the flagellated body from the crescent.

were, a small central sphere within the larger sphere. After a time in the hyaline spheres the hæmozoin particles begin—at first slowly and intermittently, afterwards more energetically—to dance about. As the movement of the pigment increases in rapidity and energy the entire sphere seems to partake in the agitation—to quiver, to change form, and to be jerked about as by some unseen force. The hæmozoin particles may now become diffused through the general mass of the sphere (Fig. 7, *d*), or they may not. Whether this does or does not happen, the agitation of the sphere now becoming intense, one or more filaments are suddenly shot out from its periphery and at once begin to indulge in characteristic waving, lashing move-

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ments (Fig. 7, *e*)*. The granular spheres do not project these filaments or microgametes.

In stained preparations it can be shown that the process of microgamete formation is preceded by fragmentation of the nucleus, the chromosomes proceeding to the periphery of the sphere and each becoming surrounded by a portion of protoplasm. The microgamete, therefore, is composed of these two elements drawn out into a thread—a chromatin filament enclosed in a covering of protoplasm. In the granular spheres there is no fragmentation of nucleus or filament formation, the minute nucleus remaining central surrounded by its circle of hæmozoin rods.

The extruded microgametes, if they do not break away as already described, may continue to move for an hour, or even longer — that is if the flagellated body be not engulfed by a phagocyte, an occurrence very frequently witnessed. Finally, they slow down, cease to move, coil up perhaps, and then gradually fade from view. Should the microgametes succeed in breaking away, the remains of the flagellated body, consisting of hæmozoin particles included in a small amount of residual protoplasm, tend to assume a somewhat spherical, passive form, the hitherto violent changes of shape and the movement of the hæmozoin ceasing almost abruptly.

In other types of malarial infection certain bodies (Fig. 8, *a*, *d*), which, but for the brisk movements of their hæmozoin, look like ordinary full-grown intracorpuscular parasites prior to the formation of spores, may sometimes be seen to slip out from their enclosing corpuscles (Fig. 8, *b*, *e*). If these free parasites are watched, in some instances the hæmozoin they contain is seen to indulge in violent dancing

* Careful focussing, especially of stained crescent-derived spheres, may sometimes show that for a short time before their eruption the microgametes exist preformed inside the limiting membrane of the sphere (Fig. 7, *e*). One can sometimes see a microgamete filament, in its efforts to erupt, carry this membrane in front of it, and, failing to break through, retract and perhaps renew the effort at another point. Doubtless, the agitated movements of the sphere are produced by the efforts made by the microgametes to break through this membrane.

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movements, the body of the parasite being at the same time agitated and jerked about. Finally, microgametes may be suddenly projected from the periphery (Fig. 8, *c*, *f*), very much in the same way as they are projected from the periphery of the crescent-derived sphere. Manifestly, these large spherical parasites and the flagellated bodies arising from some of them correspond to the crescent-derived sphere and crescent-derived flagellated body.

Conditions favouring and retarding eruption of microgametes.—Ross has shown that, provided the blood containing the crescent body be prevented from coming in contact with the air, as can be secured by pricking the finger through vaseline, evolution does not proceed. He has further shown that if the droplet

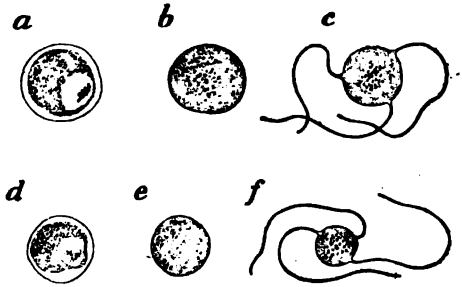

Fig. 8.—*a*, *b*, *c*, Evolution of the flagellated body in tertian fever; *d*, *e*, *f*, evolution of the flagellated body in quartan fever.

of blood is exposed to the air for a minute or two before being mounted on a slide, the eruption of microgametes is markedly encouraged. Similarly, Marshall has shown that it is also favoured by mixing the blood with a trace of water. I find that by combining these methods—namely, exposure to the air with slight aqueous admixture, as by breathing on the slip before applying the cover-glass—it is generally easy to procure quickly, from crescent-containing blood, specimens of the flagellated body. Probably, although I have not experimented with this object in suitable cases, the eruption of microgametes will be favoured in the non-crescent-forming parasites by similar means.

In certain bloods the flagellated body is easily procured; in others the opposite is the case. As regards the crescents, doubtless success depends in a measure on the degree of maturity of the parasite, young or effete crescents failing to evolve. There are other conditions affecting the process, however, which are as yet unknown.

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MOSQUITO-MALARIA THEORY

Popular and early views.—The idea that some relationship exists between the mosquito and malaria has long been entertained, not only by medical men, but also by the inhabitants of malarial countries. In parts of Italy the peasants for centuries have believed that fever is produced by the bite of the mosquito—a fact noted by Lancisi; and, as Koch has pointed out, in German East Africa the natives of the highlands declare that when they visit the unhealthy lowlands they are bitten by an insect they call *Mbu* (mosquito), with the result that they get fever which they also call *Mbu*. King and others long ago pointed out how a mosquito-malaria hypothesis could best explain such things as the connection of malaria with swamps and with high atmospheric temperatures; the well-known danger of night exposure in malarial countries; the influence of trees, of an expanse of water, and of altitude on the diffusion of the germ, and many other points. As to how the mosquito intervened they had no reasonable hypothesis to offer. Laveran, Koch, and Pfeiffer suggested that the mosquito might stand in the same relation to the malaria parasite as it stands to the larva of *Filaria nocturna;* but as to the particular phase of the parasite it subserved, and as to the exact way in which the insect operated, they were silent.

A mosquito-malaria theory definitely formulated.—In 1894 * and again in 1896, I formulated a definite hypothesis on the subject. Being a parasite, the germ of malaria, to keep in existence as a species, must pass from host to host; in other words, must at some time have an extracorporeal life. From the fact that the flagellated body does not come into existence until the blood has left the blood-vessels—that is, until it is outside the body—I concluded that the function, then unknown, of the flagellum lay outside the human body, and that the flagellated body was the first phase of the extracorporeal life of the malaria parasite. As the parasite whilst in the circulation is

* *Brit. Med. Journ.*, December 8th, 1894; "Goulstonian Lectures," *Brit. Med. Journ.*, March 14th, 21st, and 28th, 1896.

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always enclosed in a blood corpuscle, and is therefore incapable of leaving the body by its own efforts, and as it is never, so far as known, extruded in the excreta, I concluded that it is removed from the circulation by some blood-sucking animal, most probably by some suctorial insect common in the haunts of malaria. This bloodsucker I believed to be the mosquito, an insect whose habits seemed adapted for such a purpose, and whose distribution conformed to the well-ascertained habits of malaria. Further, basing my argument on what I had shown to be the fact in the case of *Filaria bancrofti*, and on the peculiarities of the distribution of malaria, I reasoned that only particular species of mosquito were capable of subserving particular species of malaria parasite.

Ross's observations.—Ross, to whom I suggested the investigation of this hypothesis, first (1895) demonstrated the fact that when crescent-containing blood is ingested by the mosquito a large proportion of the crescents rapidly proceed to microgamete formation and to the emission of microgametes. In 1897 he showed that in particular species of mosquito fed on malarial blood, living and growing malaria parasites containing hæmozoin are to be found embedded in the stomach wall of the insects. Early in 1898 (as announced by me at the meeting of the British Medical Association, in Edinburgh, in July, 1898), he showed that if a particular species of mosquito be fed on the blood of plasmodium-infected birds, the parasite, which both in habit and structure closely resembles the malaria parasite of man, enters the stomach wall of the insect, grows and sporulates there, and that the resulting sporozoites subsequently enter the salivary gland of the insect, and that the insect is then capable of infecting by its bite other birds. Ross further showed that only particular species of mosquito could subserve the avian plasmodium in this way, and that the particular mosquito in question was not efficient as regards another blood parasite of birds—namely, hæmoproteus—or as regards the malaria parasites of man. Thus by direct observation and by analogy Ross distinctly, and first, proved that the extracorporeal phase of the malaria

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parasite is passed in particular species of mosquitoes, and, by analogy, that the parasite is transferred from man to man by the mosquito.

MacCallum's discovery.—A gap in Ross's observations was filled in by MacCallum, who showed, principally by observations on hæmoproteus, also a malaria-like parasite of birds, that the function of the filament after it breaks away from the parent sphere, or flagellated body, is to impregnate (Fig. 9, *c*, *f*) the granular crescent-derived spheres, which then become

Fig. 9.—Hæmoproteus (*after Celli*).

a b c, Evolution of macrogamete; *c*, fertilisation by microgamete; *d e f*, evolution of microgamete.

transformed into sharp-pointed travelling vermicules. Doubtless, although the process has not been directly observed, it is in virtue of the locomoting and penetrating properties of the travelling vermicule that the malaria parasite is enabled to lodge itself, where Ross first found it, in the stomach wall of the mosquito.

Confirmation and extension of Ross's work.—Ross's observations were quickly confirmed and elaborated by the Italians, by Daniels, and by Koch. Grassi has shown that several species belonging to the genus *Anopheles*, more particularly—at

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all events as regards Italy—*Anopheles maculipennis*, are the special mosquito-hosts of the malaria parasites of man. Step by step he traced the crescent-forming and the non-crescent-forming malaria parasites through their mosquito hosts, finding that in their evolution they closely resembled that which Ross had so successfully demonstrated for the avian plasmodium, and had so clearly foreshadowed and partly demonstrated for the malaria parasite of man. In conjunction with Bignami he repeated successfully in man Ross's experiment of conferring malarial disease by mosquito bite. Bastianelli, Celli, Dionisi, Buchanan, and others have also succeeded in confirming Ross's statements, and in adding to our knowledge of the extracorporeal cycle of the malaria parasite.

Finally, on behalf of the Colonial Office and the London School of Tropical Medicine, with the assistance of Drs. Sambon and Low, I instituted two experiments which dispose for good and all of any objections that otherwise might have been advanced against the theory. Drs. Sambon and Low, Mr. Terzi, their servants and visitors, lived for the three most malarial months of 1900 in one of the most malarial localities of the Roman Campagna—Ostia—in a hut from which mosquitoes were excluded by a simple arrangement of wire gauze on the doors and windows. They moved freely about in the neighbourhood during the day, exposed themselves in all weathers, drank the water of the place, often did hard manual work, and beyond retiring from sunset to sunrise to their mosquito-protected hut observed no precautions whatever against malaria. They took no quinine. Although their neighbours, the Italian peasants, were each and all of them attacked with malaria, the dwellers in the mosquito-proof hut enjoyed an absolute immunity from the disease. Whilst this experiment was in progress mosquitoes fed in Rome on patients suffering from tertian malaria were forwarded in suitable cages to the London School of Tropical Medicine, and on their arrival were set to bite my son, the late Dr. P. Thurburn Manson, and Mr. George Warren. Shortly afterwards both of

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these gentlemen, neither of whom had been abroad or otherwise exposed to malarial influences, developed characteristic malarial fever, and malarial parasites were found in abundance in their blood both at that time and on the occurrence of the several relapses of malarial fever from which they subsequently suffered.

The mosquito-malaria theory has now, therefore, passed from the region of conjecture to that of fact.

THE MALARIA PARASITE IN THE MOSQUITO

(*See Fig.* 10)

In the lumen of the stomach: travelling vermicule stage.—When crescent-containing blood has been ingested by certain species of mosquito belonging to the *Anophelinæ*,* those crescents that are mature, and that are not obsolescent, are transformed into the two types of sphere already described—hyaline and granular; that is, male and female. The hyaline spheres then emit their filaments or microgametes, which, breaking away, approach and seek energetically by butting and boring to enter the granular spheres. At one point on the surface of each of the granular spheres a minute papilla is projected to meet, as it were, a corresponding attacking microgamete. At this point one of the latter contrives to enter, and, after momentarily causing considerable perturbation in the contents of the sphere, comes to rest and vanishes from view. Although the granular sphere may be subsequently energetically attacked, no second microgamete can effect an entrance. For a short time after this act of impregnation† the granular sphere or

* So far, this is the only kind of mosquito which has been found an efficient insect host for the parasite.

† The impregnation of the granular sphere has only twice been witnessed in the case of the malaria parasite of man (MacCallum); but in hæmoproteus of birds it has been observed many times. Koch has seen the resulting travelling vermicule in the plasmodium of sparrows. Analogy, therefore, justifies the inference, so compatible with the other well-ascertained features in the cycles of the intracorpuscular parasites of man and the lower animals, that a similar arrangement obtains in the Plasmodiæ of man. Prof. Grassi showed me sections of the mosquito's stomach in which the travelling vermicules could be seen approaching and actually in contact with the epithelial coat. These preparations were from mosquitoes killed thirty-two hours after feeding on malarial blood.

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macrogamete undergoes no apparent change. Presently, however, it gradually alters in shape, becoming oval, elongated, and finally assuming a lanceolate and then a vermicular form, the hæmozoin accumulating at the broad or posterior ends whilst the anterior end becomes pointed and hyaline. On the completion of these changes, the little body begins to move about; at first slowly, then more rapidly, the pointed end being in front. Should this travelling vermicule, technically known as an "oökinet," impinge on a blood corpuscle, white or red, it passes through it.

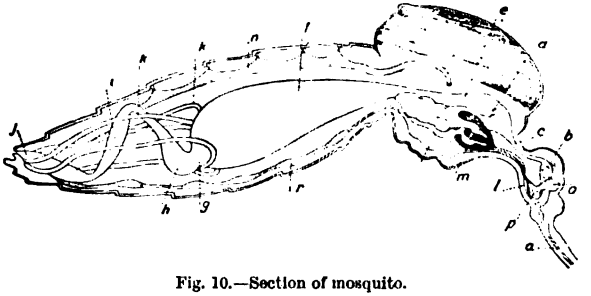

Fig. 10.—Section of mosquito.

a, mouth; *b*, pumping organ; *c*, œsophagus; *d*, homologue of proventriculus; *e*, anterior part of mid-gut; *f*, mid-gut; *g*, pylorus; *h*, pyloric diverticulum; *i*, hind-gut; *j*, rectum; *k*, malpighian tubes; *l*, salivary duct; *m*, salivary gland; *n*, dorsal vessel; *o*, supra-œsophageal ganglion; *p*, sub-œsophageal ganglion; *q*, conjoined ganglia; *r*, abdominal ganglia.

Dissection of the Mosquito.—To follow the evolution of the malaria parasite the student, by frequent dissection, should first familiarise himself with the normal appearance of the internal organs of the mosquito. The following method of obtaining and mounting the organs for microscopic examination is that taught by Dr. Daniels at the London School of Tropical Medicine. Having killed the mosquito by chloroform, tobacco smoke, etc., with a mounted needle transfix the thorax, and with the fingers pull off the legs and wings one by one, being careful to pull them obliquely from the needle. The body of the mosquito should then be placed in a drop of normal saline solution on a glass slide. Then flatten out a little the posterior end of the abdomen, and nick it on each side about the junction of the penultimate segment; a weak place in the exoskeleton is thus formed. The thorax being now fixed with one mounted needle, another needle placed flat on the last segment of the abdomen steadily drags this away from the rest of the mosquito. The stomach or mid-gut and

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malpighian tubes can thus be gradually pulled out from the exoskeleton; when sufficient length of œsophagus comes into view it can be divided by a touch of the needle. The ovaries of the female and testes of the male are also pulled out with the stomach. Sometimes the stomach is found to be full of blood or other food. In this case it is necessary to make a nick in the stomach; the weight of the cover-glass, which should now be applied, by its gentle pressure may express the blood. Occasionally it is necessary to wash the blood away, by allowing the stomach to refill with saline solution and then pressing on the cover-glass, and repeating the process as often as may be necessary.

The salivary glands, lying in the prothorax, can sometimes be obtained by pulling them out in dragging off the head. This method should be avoided if possible, as the glands are difficult to separate from the head, and it is impossible to compress the head without crushing the eyes; the pigment thus set free interferes with a microscopic examination. The simplest and most certain method of procuring the salivary glands is, after *cutting* off the head, to divide the thorax obliquely, so that its anterior portion, including the attachments of the anterior and middle pair of legs, is separated from the rest of the trunk. This portion contains both salivary glands. The exoskeleton should then be broken up with needles into five or six pieces in normal salt solution. A cover-glass is applied and steady pressure exercised with the point of the needle over each fragment of the exoskeleton. In this manner the glands are separated from the chitinous fragments, and can be readily examined. In the majority of dissections at least five out of the six lobes will be exposed undamaged.

In the stomach wall: encysted or zygote stage (Fig. 11).—This newly acquired power of locomotion and penetration on the part of the fecundated parasite, together with other well-ascertained facts, justifies the presumption that soon after its formation the travelling vermicule, now known as an "oökinet," penetrates the wall of the mosquito's stomach. Working its way through the layer of cells and the delicate basement membrane which together constitute the inner coat of this organ, it finally lodges itself among the longitudinal and transverse muscular fibres lying between this inner membrane and the equally delicate outer coat. Here the parasite, some thirty-six hours after the mosquito has fed, may be detected as a minute (6μ) oval or spherical body with a sharp outline and hyaline or slightly

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granular contents in which the hæmozoin particles are plainly visible. It lies between the muscular fibres, which, as it grows, it dissociates to a certain extent.

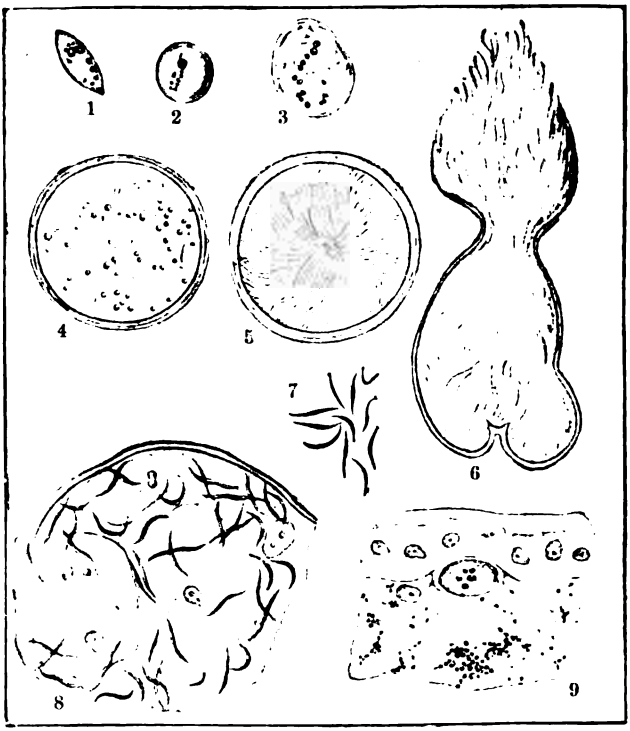

Fig. 11.—Evolution of the crescent parasite in Anopheles maculipennis. (*Adapted from Grassi, Bignami, and Bastianelli.*)

1 to 6, the parasite as found in the stomach wall; 7, isulated sporozoites; 8, sporozoites in the salivary gland; 9, section of stomach wall showing the parasite *in situ*.

During the next few days the parasite increases rapidly, acquiring a well-defined capsule, and, in consequence of its growth, protruding on the surface of the insect's stomach like a wart or wen (Fig. 12). Meanwhile, important changes take place in the interior of the parasite, which has

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now acquired a spherical contour and has attained the stage of development to which the term "oöcyst" is applied. Nucleus and protoplasm divide into a number of spherular daughter cells, around which, attached by one end like the spines on a porcupine, a vast number of minute (16μ), slender spindle-shaped, nucleated bodies are ultimately formed. At a later stage the spherules disappear, leaving the spindles, "sporozoites," loose in the capsule, which is now packed to bursting point. In about a week—sooner or later according to atmospheric temperature, which has a great influence on the rate of development of the parasite—the capsule ruptures and collapses, discharging its contents into the body cavity of the mosquito.

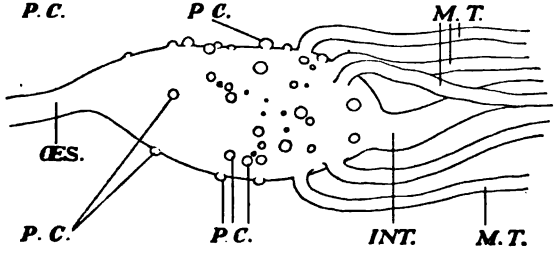

Fig. 12.—Stomach after infection with proteosoma: M.T., malpighian tubes; *Int.*, intestine; *Œs.*, œsophagus; P.C., proteosoma zygotes protruding into the body cavity.

In the salivary gland: sporozoite or infective stage.—From the body cavity of the mosquito the spindle-shaped sporozoites pass, probably by way of the blood, to the three-lobed salivary glands lying one on each side of the fore-part of the thorax of the insect (Figs. 10, *m*, and 13, B). These glands communicate with the base of the mosquito's proboscis by means of a long duct, around the radicles of which the clear, plump cells of the gland are arranged. The sporozoites can be readily recognised in many (Fig. 11, 8), though not in all, of the cells, especially in those of the middle lobe, and also free in the contents of the ducts. So numerous are they in some of the cells that the

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appearance they present is suggestive of a bacillus-laden lepra cell.

TRANSFERENCE TO THE HUMAN HOST

By a large number of experiments, abundantly confirmed, Ross distinctly proved that if appropriate birds

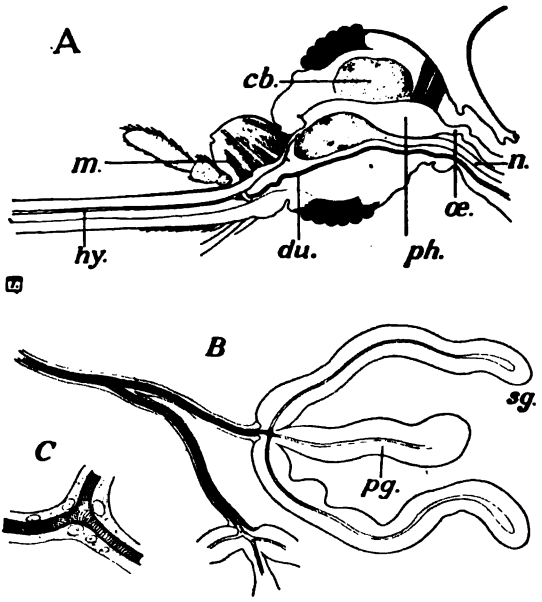

Fig. 13.—Dissection of head of mosquito.

A, Median section of head, showing *du*, the veneno-salivary duct, with its insertion in *hy*, the hypopharynx; *cb*, cerebrum; below this are the cerebellum and the pumping enlargement of *œ*, the œsophagus; *m*, muscle; *n*, nerve commissure. The other parts have been removed. B, the veneno-salivary duct, showing its bifurcation and the three glands on one of its branches; *pg*, poison gland; *sg* marks the upper of the two salivary glands. C, the bifurcation of the duct with its nucleated hypodermis.

are bitten by mosquitoes whose salivary glands contain the sporozoites of the avian plasmodium, the birds become infected with the parasite, and in due course show it in their blood and develop corresponding clinical symptoms. And now many experiments, some of which have been alluded to, have clearly

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shown that a similar process occurs in the evolution of the malaria parasite. If a mosquito whose salivary glands contain malarial sporozoites bites a

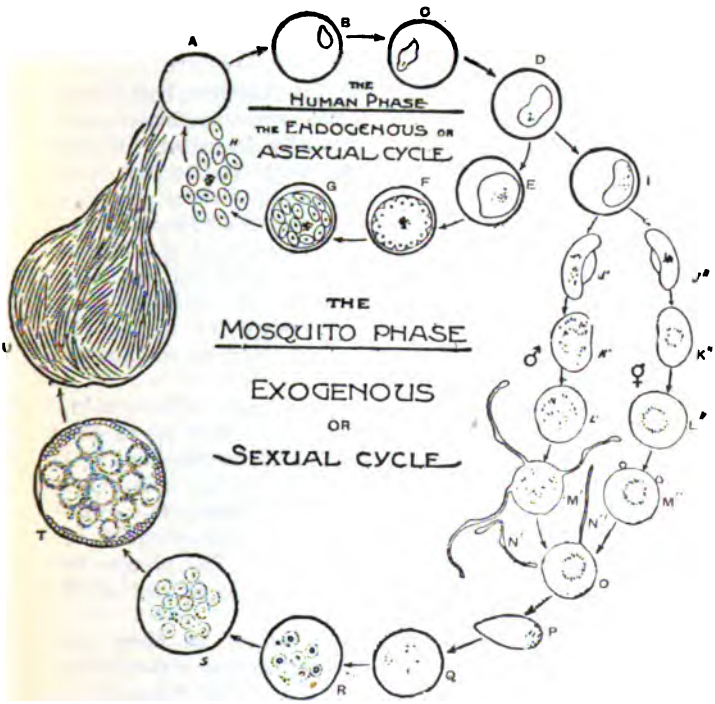

Fig. 14.—Schema showing the human and mosquito cycles of the malaria parasite. Modified from Blanchard's diagram illustrating life cycle of Coccidium Schubergi. (From the Malaria number of the *Practitioner*, March, 1901.)

A Normal red cell; B, C, D, E, red cells containing amœbulæ or myzopods; F, G, H, sporocytes; I, young gametocyte; J', K', L', M', microgametocytes or male gametes; J'', K'', L'', M'', O, macrogametocytes or female gametes; N', N'', microgametes; P, travelling vermicule; Q, young zygote; R, S, zygotomeres; T, blastophore; U, mature zygote.

man, the sporozoites are introduced into the blood, penetrate the red corpuscles, and multiply. After eight to ten days, their progeny can be seen as malaria parasites of the type corresponding to those of the man

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on whom the infecting mosquito had originally fed. Schaudinn, by diluting blood with blister serum and introducing into the mixture the salivary glands of a malaria-infected mosquito, was enabled to witness the entrance of the sporozoites into the red corpuscles.

COMPLETE CYCLES OF THE PARASITES

The complete cycles (Fig. 14), therefore, both intra- and extracorporeal, of the endocorpuscular blood parasites of man and birds can now be described. Using the most generally adopted zoological terms, and commencing with the youngest phase, these parasites may be described as entering the blood corpuscles as *sporozoites*. Growing at the expense of the hæmoglobin they become pigmented and, on reaching maturity, develop either into (*a*) *schizonts* (the segmenting body—rosette body), or into (*b*) *gametocytes* (crescents, spherical body of tertians or quartans).

(*a*) The schizonts, after concentration of hæmozoin, divide into a number of naked segments or *merozoites*, which, on the breaking down of the enveloping blood corpuscle, escape into the blood plasma and enter fresh blood corpuscles; thus completing the *endogenous cycle* and providing for the multiplication of the parasite in the vertebrate host. The process of reproduction in this the *asexual cycle* is called *schizogony*.

(*b*) The *gametocytes*, or *gametes*, as they are usually termed, belong to the *exogenous* or *sexual cycle* passed in the bodies of particular species of mosquito. They are of two kinds: *male* (hyaline crescents or spheres) and *female* (granular crescents or spheres). The male gametocyte emits several *microgametes* (flagella), one of which, breaking away, enters and impregnates the single *macrogamete* of which the female gametocyte consists. The product is a *zygote*, which, having acquired locomoting powers, becomes an *oökinet* and transfers itself from the lumen to the wall of the middle intestine (stomach) of the mosquito in which it had developed. Here it comes to rest and is soon surrounded with a capsule. It is now called an *oöcyst*.

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Presently it divides into a number of daughter cells and *residual bodies*. The former produce a vast number—as many as ten thousand in a single oöcyst—of minute bodies, the *sporozoites* (zygotoblasts, germinal rods—Ross). Finally the oöcyst ruptures, discharging the sporozoites into the body cavity of the insect, whence they are transferred to the salivary glands, in the secretion of which, opportunity offering, they are injected into the blood of an appropriate vertebrate, whose blood corpuscles they subsequently enter, and, becoming schizonts, renew the cycle. The process of multiplication in this the *sexual* or *exogenous* cycle is called *sporogony*.

POSSIBILITY OF YET ANOTHER PHASE

So far the story of the life-history of these parasites seems to be complete. There are certain facts, however, which seem to indicate the possibility of yet another phase, or of ætiological factors which hitherto have escaped observation. First, there are districts in India, Africa, and elsewhere that are practically uninhabited on account of the prevalence and virulence of the local malaria. If man be necessary for the completion of the life-cycle of the parasite, how explain its abundance in such circumstances—that is to say, in the absence of man? Second, those engaged in malarious districts on works entailing disturbance of the soil, *e.g.* opening jungle lands, digging canals or foundations, making roads or railways, are particularly prone to contract malaria; yet such operations at first sight seem in no way calculated to foster broods of malaria-infected mosquitoes. How account for infection in such circumstances? where, and in what form, is the malaria germ to be found there?

Of the first of these difficulties two explanations may be submitted. (*a*) The malaria parasite may be capable of living in a variety of animal hosts, as we know to be the case with the hæmoprotozoa of birds and many other and more highly organised animal parasites. It may be that in the malarious districts alluded to the prevalence of such

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an appropriate host, together with the presence of an appropriate mosquito, insures the continuance and abundance of the parasites. Support is given to this hypothesis by Dionisi's discovery of intracorpuscular parasites in bats, closely resembling the malaria parasites of man; and by a similar discovery by Koch in monkeys. Similar parasites have also been found in the ox, lamb, sheep, dog, and horse. (*b*) The malaria parasite may be capable of passing from mosquito to mosquito without the intervention of a vertebrate, by passage of the sporozoite into the mosquito's eggs. We have the support of analogy for this hypothesis. Several Babesiæ, such as *Babesia bovis*, which gives rise to hemoglobinuric fever (Texas fever) in cattle, and *Babesia canis*, which causes the malignant jaundice of dogs, are transmitted in this way. The intermediary, a tick, takes in the parasite with the blood it sucks from an infected animal. The parasite, probably after undergoing developmental changes, then passes into the egg of the tick and so to the young tick hatched out from the infected egg, and it is this young tick that implants the germ into the next vertebrate host. In the case of the trypanosoma of the little owl, Schaudinn claimed to have shown that it may enter the eggs of the intermediary mosquito and that the infection may in this way be transmitted, not only by the mosquito that sucked the trypanosoma containing blood but also by its progeny.

Most observers are now of opinion that the malaria parasite, under natural conditions, can be acquired by man only through the bite of the mosquito; that the mosquito can acquire the parasite only by ingesting the blood of a malaria-infected man or, possibly, other mammal; that there is no extracorporeal life other than that described; that there is no authentic instance of malaria being acquired in uninhabited places; that in the case of malaria in connection with soil disturbances, it depends on the creation during digging operations of puddles of water in which

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mosquitoes breed; and that its epidemic occurrence under these circumstances is owing to unhygienic conditions, such as usually prevail when large bodies of men, some of whom may bring the infection with them, are brought together on public works attended with extensive earth cutting, as in railway, road, or canal making.

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CHAPTER II

MALARIA: THE MICROSCOPICAL EXAMINATION OF THE BLOOD

BEFORE commencing the study of malarial blood it is advisable for the beginner to familiarise himself with the microscopical appearances of normal blood, both in fresh and stained preparations. He should learn to recognise the several varieties of leucocyte; to appreciate differences in colour, size, and shape of the red cells; to recognise dirt, vacuoles, forms of crenation, and artificially produced appearances. By mastering such details at the outset important sources of fallacy will be avoided, and in the process of self-education a useful knowledge of technique will be acquired. The English-reading student will find the works of Coles, of Cabot, and of da Costa of great assistance.

For a thorough appreciation of the principles on which blood examinations for the demonstration and study of the malaria parasite should be conducted, it must be borne in mind that the parasite is intra-corpuscular. To see it, therefore, it is necessary, particularly for the beginner, so to dispose the corpuscles in the preparations that a proportion of them shall lie flat on the slide, in a single layer, and presenting their surfaces, and not their edges, to the observer (Fig. 15). It is mainly from ignoring this fundamental principle that so many fail to find the parasite.

Preparation of fluid blood films.—To secure this disposition of corpuscles in fresh blood the following procedure, the smallest details of which must be scrupulously carried out, is recommended :—

Thoroughly cleanse with alcohol three or four thin cover-glasses and as many slips, and cover them immediately with some convenient vessel so as to protect them from the minutest particle of floating dust. Cleanse one of the patient's

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finger-tips with alcohol and dry it. Prick the part with a clean needle, and wipe away the first drop of blood that exudes. Then gently, with finger and thumb, squeeze the finger-pad and express a second minute droplet of blood; this should be very small—no larger than a pin's-head. Touch the droplet lightly with the centre of a cover-glass, taking care that the latter does not come into contact with the skin, and immediately drop the cover-glass on the slide. No pressure should be used to cause the blood to spread out. If glasses

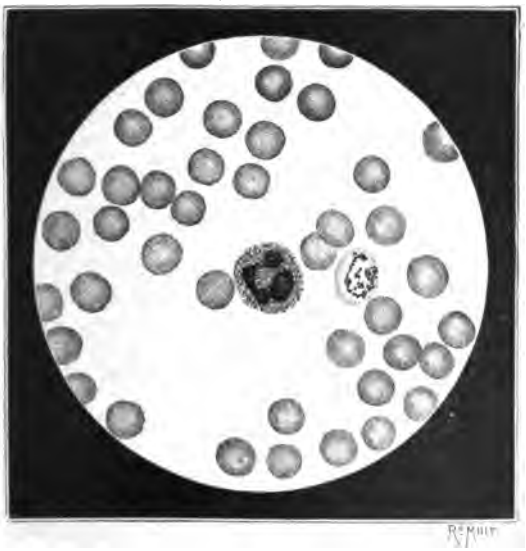

Fig. 15.—Microphotogram showing the necessary disposition of blood corpuscles in slides for examination for the plasmodium. To the right of the white blood corpuscle in the centre of the field a red blood corpuscle three-fourths filled with a tertian parasite is visible. (*From microphotogram by Dr. Cosens.*)

and skin are quite clean, the blood will at once run out in a very fine film. It is sometimes more convenient to obtain the blood from the lobe of the ear or, in children, the great toe.

Several preparations should be made, the requisite blood being obtained by renewed gentle compression of the finger-tip.

After waiting a few minutes to allow the blood to spread out completely between the glasses, it is well

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to ring the preparations with vaseline. This will effectually stop all movement, all evaporation of the blood, and, consequently, over-compression of the corpuscles, and will thereby greatly facilitate examination.

In making these preparations care should be taken to sterilise the needle employed, otherwise grave accidents might occur. It is, of course, unnecessary to sterilise the slides and cover-glasses.

Characteristics of a successful preparation.—On holding a successful preparation up to the light, one or more areas, each made up of three zones, the different zones shading into each other, can be made out by the naked eye. Each such area includes a peripheral zone of a reddish tinge, a middle zone having a somewhat iridescent look, and a central zone absolutely devoid of colour. Successful preparations may be recognised by the presence of these zones. Preparations not exhibiting this appearance should be rejected; it is waste of time to examine them.

On examining successful preparations with the microscope, it will be found that the central zone or area contains few or no blood corpuscles. This zone may be designated the "empty zone." Proceeding outwards from this we come on an area occupied by scattered, isolated, compressed, and much-expanded corpuscles — the "zone of scattered corpuscles." Farther out the corpuscles become more numerous and less expressed (Fig. 15). Gradually, as we trace the film still farther outwards, the corpuscles are found approximated to each other, until, finally, the peripheries of the corpuscles are mostly in touch —the "single-layer zone." Farther out the corpuscles, though still lying flat, are found to overlap each other or are piled one on the top of the other— the "zone of heaped-up corpuscles." Beyond this zone the corpuscles are arranged in rouleaux—the "zone of rouleaux." At the extreme margin of the preparation the corpuscles tend to break up and run together so as to form a narrow border of free hæmoglobin, the individual corpuscles, perhaps, being indistinguishable—the "zone of free hæmoglobin."

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Each of these zones should be studied, for each may afford special information about the malaria parasite.

Microscopical examination.—The beginner will save time if he gets someone who is familiar with the necessary technique, and with the appearance of the parasite in the blood, to give him one or two lessons. Accuracy and quickness can be acquired only by practice. It is a good plan to practise preparing films from one's own blood.

The examination is best conducted with $\frac{1}{12}$ of an inch oil immersion lens, a rather low eyepiece, a sub-stage condenser, and a good but not too dazzling illumination. It is practically useless to work with any objective lower than $\frac{1}{12}$, or without a sub-stage condenser.

It is not always possible to choose, but, if practicable, a case of quartan infection should be selected for examination in the first instance. Failing a quartan, a well-defined benign tertian infection might be chosen. Failing either of these, a long-standing case of recurring malaria with marked cachexia will afford the next best opportunity. It is best to examine the patient's blood just before or at the time of rigor. In quartans and benign tertians, at the time named, there should be little difficulty in discovering large parasites; in the case of these infections attention is called to the relatively large parasites by the abundance of coarse pigment they contain. In the blood of malarial cachectics with recurring febrile attacks it is generally an easy matter to find crescents and crescent-derived spheres, as this form of the parasite is of considerable size, carries abundance of pigment, and possesses a very definite and striking shape.

When the beginner has learnt to recognise the larger forms of the parasite, he will have begun to appreciate what sort of body he has to look for; thereafter he should be able to educate himself, and to pick out the smaller and intermediate forms.

In proceeding to make his first examination of a liquid blood slide, the beginner, in the first instance, should confine his attention to the "single-

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layer zone." Field after field of this he must pass in review, carefully scrutinising the interior of every blood corpuscle, every leucocyte, and every pigmented body, even though it be not included in a corpuscle. He must not expect to find parasites in every corpuscle, or even in every field; and he certainly must not expect, as the beginner usually does, to find in every slide the beautifully regular segmenting form or "rosette body" or the weird-looking flagellated body made familiar to us by so many illustrations. Such bodies, though really present somewhere and in some form at one time or another in every case, are among the least common of the many phases of the malaria parasite; they are met with only under very definite and not very constantly encountered conditions, and are not very often seen at an ordinary clinical examination.

In most cases the parasite is discovered in the first field or two examined; but in not a few instances dozens of fields may have to be scrutinised before a single parasite is found. Therefore no examination can be said to be complete, in a negative sense, until at least half an hour has been spent over several suitably prepared slides.

The intracorpuscular forms most frequently met with have the appearance either of small specks of pale protoplasm, or of larger masses of pale protoplasm containing grains of black pigment. Close watching discovers that the former are endowed with amœboid movement, and that they continually change shape and position in the affected corpuscles. As these movements are an important test of the parasitic nature of the body sought, they should be carefully looked for. The smallest protoplasmic specks look like washed-out smudges of dirty white paint, half hidden by the hæmoglobin; they are sometimes hard to see. Their parasitic nature can readily be determined by their movements; by their soft, ill-defined margins; and by the fact that they tend now and again, on first removal from the body, and permanently later, to assume the appearance of tiny white rings which show up very distinctly in the

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hæmoglobin of the corpuscle. These features readily distinguish them from the sharply defined, clear, motionless, non-parasitic vacuole (Fig. 16). The other common forms—the larger or smaller intracorpuscular pigmented parasites—occupy anywhere from a sixth to nearly the entire area of the affected corpuscles. They are recognised by their pale protoplasm; by the black hæmozoin particles scattered about or, if towards the period of rigor, concentrated in their interior; and by their more or less active amœboid movements. In quartans and tertians, but especially in the former, segmenting rosette forms are seen occasionally.

Examination of blood for flagellated bodies.—When the student has become familiar with these appearances, and has thoroughly seized the fact that the segmenting forms are to be found only, or usually, during, just before, or soon after the rigor stage of fever, he should endeavour to follow up the initial steps of the exogenous, sexual or mosquito phase of the parasite. So far as ordinary preparations permit, this phase is best studied in the "zone of heaped-up corpuscles" and in the "zone of rouleaux"; because in these zones the parasite, not being subjected to pressure, has more freedom to undergo its evolutionary change into the flagellated body.

In ordinary quartans and tertians flagellated bodies are but seldom encountered. The best time to find them in such cases is said to be during the hot stage of the fever. In cases of crescent infection they are much more frequently met with, as, in this form of malaria, flagellated bodies are usually more numerous, appear at any time of the clinical cycle, and persist in the circulation perhaps for several weeks after fever has disappeared.

In most cases of crescent infection the gradual evolution of the flagellated body from crescent through oval and sphere can, with patience, be easily followed.

Diagnostic value of the "zone of free hæmoglobin."—The zone of free hæmoglobin is of value as enabling the practised observer to pronounce very rapidly on the presence or absence of pigmented

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parasites in the blood. The relatively large quantity of blood in each field of this zone, and therefore the proportionally large number of parasites in any given field, lends itself to this, as does the fact that the hæmozoin shows up very distinctly in the homogeneous sheet of free hæmoglobin.

Phagocytosis and pigmented leucocytes.—Striking examples of phagocytosis are often witnessed in malarial blood. So soon as a malarial parasite, whether spontaneously or as a result of pressure, escapes from the blood corpuscle in which it had developed, it becomes exceedingly liable to attack by the phagocytes. More especially is this the case with the flagellated organism; this body seems to have a powerful attraction for the phagocytes, which are often seen to travel long distances to attack it.

Pigmented leucocytes—that is to say, leucocytes containing grains or blocks of hæmozoin—are very often encountered; they can best be seen in the single-layer zone during, or shortly after, fever. Leucocytes may sometimes be observed to include the hæmozoin set free by the falling to pieces of the segmented parasites. Often they derive their hæmozoin from the remains of some sphere or flagellated body which they may have engulfed subsequently to the preparation of the slide. In peripheral blood the phagocytes are rarely, if ever, seen to attack the parasite so long as it is inside a blood corpuscle.

Both the large mono- and, very rarely, the polynucleated leucocytes may contain malarial pigment. Care, however, must be exercised in drawing conclusions from the discovery of black material in these bodies; in imperfectly cleaned slides, fragments of dirt, which the leucocytes rapidly take up, are apt to mislead.

Pigmented lymphocytes.—According to Metschnikoff, the lymphocyte has no phagocytic action in malaria. This observation I believe to be correct. Several writers, however, have described and figured what they regard as malarial pigment in the lymphocyte. This, I am convinced, is founded on an error in interpretation, and has arisen from ignorance of the fact that in all bloods, healthy and malarial alike,

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from 20 to 50 per cent. of the small mononucleated lymphocytes contain, lying in the narrow zone of cytoplasm, one or two minute round dots of intensely black material optically indistinguishable from hæmozoin. I am not aware that this appearance has been described hitherto, but multiplied observation has convinced me of the accuracy of my statement. The discovery, therefore, of what looks like a speck of intensely black pigment in the lymphocytes must not be regarded as evidence of malarial infection.

Diagnosis of vacuoles.—The beginner may have a difficulty in determining whether certain appear-

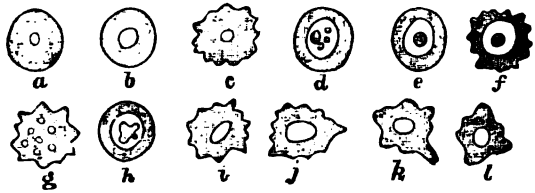

Fig. 16.—Vacuolated and crenated blood corpuscles. (*After Laveran and Blanchard.*)

a, *b*, *c*, Blood corpuscles with central vacuoles, *c* is crenated; *d*, *e*, *f*, *h*, blood corpuscles with central vacuole containing fragmented hæmoglobin. Sometimes minute eye-shaped vacuoles with a speck of hæmoglobin in the centre are met with, and are apt to be taken for parasites. *g*, crenated blood corpuscles with several vacuoles, or it may be, crenations out of focus; *i*, *j*, *k*, *l*, deformed blood corpuscles with central lacunæ.

ances in the corpuscles are vacuoles, or whether they are parasites. The following hints may help him to a correct decision. Vacuoles (Fig. 16, *a*, *b*, *c*, *d*, *e*, *f*, *h*, *i*, *j*, *k*, *l*) are well defined, clear, and have sharp edges; they may change form slightly, but they have no true amœboid movement, carry no pigment, and, of course, do not stain. Intracorpuscular malaria parasites, on the contrary, are dim and, as a rule, ill-defined; they have soft, shaded-off edges; possess amœboid movements; when large they carry hæmozoin grains; and, of course, they take the appropriate stains. It is hardly necessary to indicate the points of diagnosis from leucocytes, or from cupped, folded, or crenated (Fig. 16, *c*, *f*, *g*, *i*, *j*, *k*, *l*) corpuscles.

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Moribund and fragmented parasites.—Moribund—it may be fragmented—free parasites (Fig. 17) are often a source of confusion to the beginner. Their nature is frequently misunderstood; they are sometimes erroneously termed "sterile bodies," an expression at one time frequently applied to the crescent-derived spheres (gametocytes). They are, in fact, mechanically-freed parasites expressed from blood corpuscles by the compression to which the blood is subjected between slip and cover-glass. The longer blood is on the slide—particularly if evaporation be not prevented by vaseline-ringing of the cover-glass—the more closely will the cover-glass approximate to the slip, the greater will be the pressure on, and consequent thinning and spreading

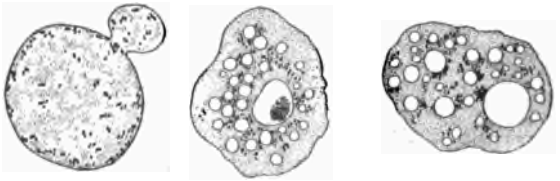

Fig. 17.—Degenerating vacuolated plasmodia.

out of blood corpuscles and parasites, and the greater the liability to damage of these very delicate bodies. Frequently the artificially-freed parasites are broken into small fragments. The entire, as well as the fragmented parasites, on becoming free in the liquor sanguinis, tend to assume a spherical or disc-like form; at the same time the protoplasm of which they are composed seems to become diffluent, and the hæmozoin is resolved into a number of minute dust-like particles possessing active, brownian movement. Some of the spherical or disc-shaped bodies with dancing hæmozoin particles are really crescent-derived spheres or other forms of gamete. These are parasites which have escaped from corpuscles in a normal way, but which have become arrested in their evolution in consequence of the abnormal conditions in which they are placed *in vitro;* others are the remains

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of flagellated bodies, the microgamete filaments having broken away.

The parasite as a means of diagnosis.—All of these multiform appearances the student must learn to recognise and interpret. Skill in this is merely a matter of time, practice, and reflection. Given these, the student should be able not only to diagnose by the microscope malarial infection, but also to recognise the type of any particular infection, the period of the fever cycle, and, it may be, the severity of the case. For diagnosis in malaria, therefore, skill in the microscopic examination of the blood is of the utmost value, and no pains should be spared by the practitioner in malarious countries to acquire it. In acute untreated malaria the parasite may be detected practically in every case. Thus in 616 cases Thayer and Hewetson—except in two or three instances where the patient's blood was examined only during convalescence—found it in every instance. The best authorities are equally emphatic on this point. Personally, I can assert that since I became familiar with the subject I have never failed to find the parasite in any acute untreated malarial case I have had a proper opportunity of examining. Whenever in a case of acute disease, supposed to be malarial, I have failed to do so, the case has turned out to be of quite another nature.

Bearing of quinine on microscopical diagnosis.—It is of little use to examine the blood for the intracorporeal forms of the malaria parasite after full doses of quinine have been taken; the drug rapidly brings about the disappearance of this phase of the parasite. The crescent alone is unaffected by drugs, and in suitable cases may be found for days after the patient is cinchonised.

On staining malarial blood.—As a general rule, the beginner should work only with unstained preparations of fresh liquid blood. To the unpractised, staining is full of pitfalls. In such circumstances it must not be relied on for purposes of responsible diagnosis. To the experienced microscopist and diagnostician, and for the study of the morphology of the

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parasite, staining is of the highest value; moreover, some such method must be employed should permanent preparations be desired, or should it be inconvenient to make an immediate examination of the blood. Many methods have been devised; here only one or two can be given.

Preparing the film.—It is usual to spread the blood on cover-glasses; for many reasons I prefer to

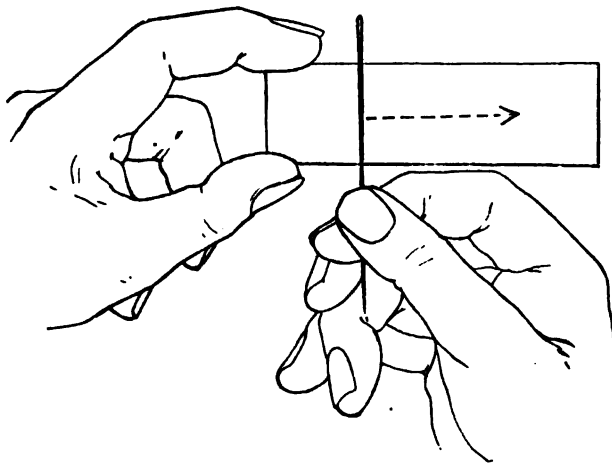

Fig. 18.—A method for the preparation of blood films. (From the Malaria number of the *Practitioner*, March, 1901.)

spread it on slips. There are various ways of preparing the films; the following I can recommend:—

Probably the easiest, as well as the quickest and most convenient, is a modification of that recommended by Christophers and Stephens. Prick the cleansed finger pad or lobe of the ear, and express a droplet of blood. Take this up by touching it lightly with a clean glass slip about an inch from one end of the slip. Across the slip and on the blood lay the shaft of the needle—an ordinary straight, rather long sewing needle (Fig. 18). Pause for several seconds

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until the blood has run out by capillarity between the needle and the slip; then, holding it by one end, push the needle over the face of the slip in the direction of the length of the latter, so as to spread the blood over the entire breadth of the middle third of the slip. By passing the soiled needle through the lapel of the coat, the operator can cleanse it quickly and be ready to make, by a repetition of the manœuvre, a series of films from the same puncture.

However spread, after the blood has dried, whenever it is desired to stain it, either at once or at any future and more convenient time, it should be "fixed" by dropping on the film a little absolute alcohol and ether in equal parts, or absolute alcohol alone. Cover-glass films may be dropped into a small wide-mouth bottle containing the fixing agent, or they may be fixed by passing them through the flame (not a good method), or by placing them for some hours (one to three) in a warm dry chamber at a temperature of 105° to 120° C. When alcohol is used, after ten to thirty minutes or longer, it must be dried off before staining.

STAINS

The stains usually employed belong to two categories: (*a*) those which stain the protoplasm and the nucleus the same colour; (*b*) those which, by tinting them differently, differentiate the protoplasm from the nucleus.

(*a*) Of the former I would recommend the following:—

Borax-methylene blue.—A drop or two of aqueous solution of borax- (5 per cent.) methylene blue (2 per cent.) is spread on the film. After thirty seconds or less the slide is thoroughly washed in water, dried with filter paper, and afterwards by gently warming over the spirit lamp. Finally, xylol balsam and a cover-glass are applied.

Loeffler's methylene blue.—Concentrated alcoholic solution of methylene blue 30 parts, solution of caustic potash ($\frac{1}{10000}$) 100 parts. Stain for thirty seconds, wash in water, dry and mount.

Carbol thionin.—Saturated alcoholic (60°) solution of thionin 20 parts, watery solution (2 per cent.) of carbolic acid

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100 parts. The mixture should be kept at least a fortnight before use. Stain for five minutes, wash and mount.

Hæmatoxylin and eosin. — Ehrlich's acid hæmatoxylin, or strong solution of hæmalum, five minutes; weak eosin, half-a-minute; wash in tap water and then in distilled water; dry and mount in xylol balsam. This is an easily carried out and effective method of obtaining less intensely stained, but more permanent preparations.

(*b*) The many methods of obtaining differential staining of protoplasm and nucleus depend on the circumstance that when solutions of certain kinds of methylene blue and eosin are mixed, a third red dye, with a special affinity for chromatin, is formed. They are all modifications of the original Romanowsky method. They are a little uncertain and troublesome to use, their success depending on the purity of the chemicals employed and careful attention to detail. The beginner is advised to become proficient, in the first instance, with the simpler methods given above. Having attained this, he should practise some form of the Romanowsky method, for, besides displaying the intimate structure of the malaria parasite, in consequence of the intense tinting of the nucleus which it effects, it greatly facilitates the finding of the smaller forms of the parasite, not always an easy matter, especially in the case of the very minute young sub-tertian or malignant parasite. Of the three methods given below, Leishman's, everything considered, is the best. Both it and Jenner's method have the advantage of dispensing with preliminary fixing.

Romanowsky's method. — Cover-glass films are fixed by heat—110° C. for one hour. They are then immediately *floated* for over two hours on a freshly prepared mixture of saturated watery solution of methylene blue, 2 parts, and watery solution of eosin (1 per cent.), 5 parts, washed in water, dried and mounted. The precipitate formed by the mixture must not be filtered out.

Jenner's stain.—Special care must be taken that there is no trace of alkali or acid on the glass on which the film is spread; it must, therefore, be washed in distilled water and stood in absolute alcohol. The stain is made by dissolving Grübler's water-soluble eosin (yellow shade) and medicinal methylene blue in pure *absolute* methylic alcohol, which must be free from acetone and other impurities; the solutions are then mixed in

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the proportions of 125 parts of ½ per cent. solution of the eosin, and 100 parts of ½ per cent. solution of the methylene blue. Or the compound body formed by the eosin and methylene blue in this mixture may be purchased in the dry state and subsequently dissolved in absolute methylic alcohol. To use the stain, a few drops are poured on the blood film and covered to prevent evaporation and precipitation. In three minutes, or a little longer, the stain is rapidly poured off, and afterwards the film is washed in *distilled* water from five to ten seconds until it assumes a pink colour. It is then dried high over the flame, or in the air, and mounted in xylol balsam.

Leishman's stain. — Two solutions are prepared. *A*, a 1 per cent. solution of medicinal methylene blue (Grübler) in distilled water, rendered alkaline by 0·5 per cent. sodium carbonate. Heat this to 65° C. for 12 hours, and allow it to stand at room temperature for 10 days. *B*, eosin, extra B.A. (Grübler), 1 in 1,000 of distilled water. Mix equal volumes of *A* and *B* and stand for 6 to 12 hours, stirring occasionally. Collect the flocculent precipitate in a filter, and wash with distilled water. Dry and powder the filtrate, which has a green metallic lustre, and contains the active ingredient of the Romanowsky stain. (This powder has been placed on the market, and can be procured in condensed tablets called *soloids*.) Make a 0·15 per cent. solution of the dye in methylic alcohol and keep in a stoppered bottle.

To use the stain, drop three to four drops of the solution on the unfixed blood film. After about half a minute to one minute or longer add six to eight or more drops of distilled water and mix them by moving about the slide. A precipitate forms at once in the water in successful slides. After five minutes or longer wash off the stain with distilled water, leaving a few drops of the water on the film for over a minute. Dry without heat, and mount in xylol balsam.

Giemsa's stain.—Azur II., eosin 3·0 grammes; azur II., 0·8 gramme, dried, powdered, and dissolved in 250 grammes glycerine, to which is subsequently added 250 grammes methyl alcohol; heat to 40° C. Shake the mixture and stand for twenty-four hours and then filter.

Fix the films in methyl alcohol (3 minutes). The staining solution is prepared by adding 1 drop of stain to 1 c.c. of distilled water at 30° to 40°. Immerse the film in this for fifteen minutes, wash in stream of water, dry, and mount in balsam.

Staining the flagellated body.—A sheet of thick blotting-paper, having rows of oblong holes (1 inch by ⅜ inch) cut out in it, is prepared; it is slightly but sufficiently moistened with water, and laid smoothly on a sheet of window glass.

A patient in whose blood the crescent form of the parasite abounds is selected. His finger is pricked and a droplet of blood, the size of a large pin's head, is expressed. A clean microscope slip is then breathed on once, and the droplet of blood immediately taken up by lightly touching it with the

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centre of the breathed-on surface of the slip. The blood is now rapidly and somewhat unevenly spread out with the needle so as to cover an area of about ¾ inch by ½ inch. The slip is immediately inverted over one of the blotting-paper cells and pressed down sufficiently to secure thorough apposition of the slip to the paper, without, at the same time, bringing the blood into contact either with the moistened paper forming the wall, or with the glass forming the floor of what is now a very perfect moist chamber. The rest of the paper cells are rapidly covered with blood-charged slips prepared in the same way. In from a quarter to three-quarters of an hour the slips are removed and dried by gently warming them over the spirit lamp—blood surface away from the flame. When dry the films are fixed with absolute alcohol, a few drops being poured on each. After ten minutes the alcohol is dried off, and a few drops of weak acetic acid (10 to 20 per cent.) are laid on the films and left there long enough thoroughly to dissolve out all the hæmoglobin. The slides are then washed in water and dried. They may now be stained with various re-agents. So far, I have obtained the best results from weak carbol-fuchsine (20 per cent.) and prolonged staining. The stain is dropped on the slip and covered with a watch-glass; after six to eight hours it is washed off with water, the slide dried, and a cover-glass applied with xylol balsam.

On examining with a twelfth immersion lens slides prepared with methylene blue,* the nuclei of the white corpuscles are seen to be very deeply stained, the protoplasm of the white corpuscles is very lightly stained, whilst the parasites are stained an intermediate tint, and show up sharply enough in the faintly tinted red blood corpuscles (Figs. 2, 15, 19). Contrast staining with eosin is uncertain in its results in methylene blue preparations; even in practised hands good preparations are the exception. For ordinary purposes I do not recommend it; it is superfluous, troublesome, and unreliable.

On examining successful slides prepared by any of the Romanowsky methods, the red blood cells will be found to be stained pale pink or greenish; the polynuclear leucocytes will show nuclear network ruby-red, the margins of the nuclei being sharply defined, whilst the protoplasm is unstained, except such

* When it is not intended to preserve the slides, a cover-glass may be dispensed with, and the immersion lens used with only the cedar oil between it and the film. For purposes of diagnosis this suffices, and much time and material are saved.

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fine eosinophil granules as it may contain, which are red; the mononuclears and lymphocytes have sharply defined ruby-red nuclei and faint blue protoplasm; the coarse-grained eosinophiles have a less deeply stained ruby-red nucleus and pale pink granules; the basophiles have dark purple-black granules and ruby-red nucleus; nucleated red cells have almost a black and sharply-defined nucleus; the blood-plates are deep ruby-red with spiky margins and sometimes a pale blue peripheral zone. The body of the malarial parasite is stained blue and the chromatin of the nuclei ruby-red; and, in deeply-stained preparations of the tertian parasite, the hæmoglobin of the including red blood corpuscles will be dotted over with certain fine or coarse red granules known as Schüffner's dots.

In preparations intended to display the flagellated body most of the slides will show numbers of spheres and several or many well-stained flagellated bodies (Figs. 3, 4, 7). Very few crescents remain untransformed. If the slips are removed and dried in from five to ten minutes after being placed on the blotting-paper cells, only crescents, ovals, and spheres will be found; if they are left for three-quarters of an hour to an hour, free microgametes and residual masses may also be found, the latter sometimes enclosed in phagocytes. Occasionally flagellated bodies are found partially included in phagocytes. Preparations stained with carbol fuchsin, as above described, make, when successful, beautiful preparations, but they do not differentiate the chromatin of the nuclear elements. To show this, some form of the Romanowsky method, preferably Leishman's or Giemsa's, must be employed.

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CHAPTER III

DESCRIPTION OF THE MALARIA PARASITES AND THEIR ASSOCIATED FEVERS

THE different clinical types of malarial disease are associated with different and corresponding species of malaria parasites.

Principles of classification of parasites. —The different species have been classified according to—

1. The duration of their respective life-cycles inside the human body.
2. Their morphological characters.
3. The clinical phenomena they give rise to.
4. The results of inoculation experiments.

It may be said that, so far as these tests go, there is evidence of plurality of species. That is to say, a particular clinical type of malarial disease is associated with a parasite of definite morphological form and intracorporeal life-cycle, characters which are maintained when the parasite has been inoculated experimentally.

In the treatment of this subject the classification suggested by Mannaberg will be followed, a classification based principally on the investigations of Golgi, Marchiafava, Bignami, Celli, Grassi, and other Italians, as well as on his own most excellent work.

The forms of the malaria parasite, and of the diseases they give rise to, may be divided into two comprehensive groups—the *benign* and the *malignant*. A principal morphological distinction between these two groups is that, whereas the benign parasites never form crescent bodies, the malignant parasites, or at least the most important of them—the sub-tertian—form crescents; that is to say, the gamete of the benign parasites is a sphere or disc, that of the

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malignant parasites a crescent. A principal clinical difference between the two is that whereas the benign parasites rarely give rise to pernicious attacks, the malignant parasites frequently do.

The benign parasites are of two kinds: One, the *quartan parasite*, having a cycle of seventy-two hours, causing a fever recurring every three days—*quartan fever;* the other, the *tertian parasite*, with a cycle of forty-eight hours, causing a fever recurring every two days—*tertian fever.*

The malignant parasite has three forms, perhaps more*: a pigmented parasite, the *sub-tertian*,† of forty-eight, or approximately forty-eight hours' cycle; a pigmented parasite—*pigmented quotidian*—of approximately twenty-four hours' cycle; and an unpigmented parasite—*unpigmented quotidian*, also approximately of twenty-four hours' cycle.

We may arrange them thus:—

Benign	Quartan Tertian	Do not form crescents.
Malignant	Sub-tertian: Form crescents.	
	Quotidian—pigmented Quotidian—unpigmented	Supposed to form crescents.

Clinical classification.—Formerly, classification being based entirely on clinical phenomena, malarial diseases were divided into quotidian, tertian, and quartan intermittents or agues, and

* Many authorities refuse to recognise more than one species of malignant parasite, the differences in length of cycle and pigmentation described in the text being regarded merely as variations depending on circumstances, and not as specific differences.

† This parasite has received several names, none of them quite appropriate. Thus the Italians call it "æstivo-autumnal," a term appropriate enough in Italy where the infection is acquired only during the summer and autumn months, but manifestly inappropriate in the tropics, where it may be acquired at any season. Koch calls it the "tropical parasite," a name equally unsuitable, seeing that the range of the parasite embraces countries far beyond the tropic belt. The term "sub-tertian" I have adopted, following Sambon's suggestion. It implies no error either as regards clinical habit, seasonal or geographical range, and it has the additional recommendation of approximating to the name hemi-tertian, applied by Hippocrates and the ancients to the class of fevers it gives rise to.

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remittents. But since it has been found that what was designated remittent fever is produced by either quartan, tertian, sub-tertian, or by quotidian parasites—the fact of intermittency or remittency being more or less a matter of accident—it has been considered advisable to expunge the term remittent fever as indicative of a distinct species of malarial disease. Any one of the five kinds of parasites enumerated may cause what was known as remittent fever. The intermittency or remittency of any given fever depends, in great measure, on the simultaneousness or the reverse of the maturation of the swarm of parasites giving rise to it. If all the parasites present are of nearly the same age, they mature approximately simultaneously and we have an intermittent; if they are of different ages, they mature at different times scattered over the twenty-four hours and we have what was known as a remittent. Further, two generations of tertian parasites maturing on successive days will produce a quotidian fever, *Tertiana duplex;* two generations of quartan parasites maturing on successive days will produce fever fits on two successive days followed by one day of freedom, *Quartana duplex;* three generations of quartan parasites will produce what clinically appears to be a quotidian fever, but in reality is a *Quartana triplex.*

Present classification not final. — The classification adopted must not be accepted as final; at best it is merely provisional. In actual practice it may be hard, often impossible, to bring the cases met with into exact line with such an arrangement. Moreover, as this classification is based in great measure on observations made in very limited districts, principally in Italy, and principally on Roman fevers, it may not apply to the entire malarial world. That it lies on a substratum of fact there can be no doubt; nor can there be much doubt that it has in many particulars a general application to malarial disease as found all over the world. Still, judging from clinical facts, there seems ground for believing that there are other species or

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varieties of the malaria parasite besides those described by the Italians, and that the list here given will have to be enlarged or recast in the future. Men with extensive experience of malarial disease in their own persons tell us that they can discriminate by their sensations and symptoms between the fevers of different localities. Analogy would incline us to believe that clinical differences of this sort depend on differences in the determining parasites.

CLINICAL PHENOMENA OF MALARIAL FEVER

Before proceeding with a description of the various malaria parasites and their associated fevers, there are certain generalities which, to save repetition, had better be mentioned here.

Intermittent fever or ague.—Every typical malarial fever is made up of a series of pyrexial attacks which recur at definite intervals of twenty-four, forty-eight, or seventy-two hours. Each attack consists of a stage of rigor, a stage of heat, and a stage of sweating; these are followed by a period, "the interval," of apyrexia—actual or relative. The duration and intensity of the constituent stages vary considerably. On the whole, they observe a certain proportion to each other; as a rule, the more pronounced the rigor, the higher the fever and the more profuse the sweating. Such attacks, with well-marked intervals of apyrexia, are designated intermittent fevers or agues. The expression "ague" is applied only to intermittents having a pronounced rigor stage.

Premonitory stage.—Before rigor sets in, and sometimes for several days before the actual disease declares itself, there may or there may not be a premonitory stage marked by lassitude, a desire to stretch the limbs and to yawn, aching of the bones, headache, anorexia, perhaps vomiting, perhaps a feeling as of cold water trickling down the back. If the thermometer be used, it will be found that body-temperature has begun to rise, it may be some two or three hours before the other and more striking symptoms which ensue set in; or it may be that the threatened attack will subside spontaneously without

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culminating in the more pronounced phenomena of a fully developed ague.

Cold stage.—When rigor sets in, the feeling of cold spreads all over the body, becoming so intense that the teeth chatter and the patient shivers and shakes from head to foot. He seeks to cover himself with all the wraps he can lay hands on. Vomiting may become distressing. The features are pinched, the skin is blue and cold-looking, the fingers are shrivelled. But the feeling of cold is entirely subjective; if the temperature be taken, it is found to be already several degrees above normal, and to be rapidly mounting. In young children it is not at all unusual to have a convulsive seizure at this stage; a fact that has to be borne in mind, as it is very apt to lead to ideas of epilepsy.

Hot stage.—After a time the shivering gradually abates, giving place to, or alternating with, waves of warmth and, before long, to persisting feelings of intense heat and febrile distress. The wraps, which before were so eagerly hugged, are now tossed off; the face becomes flushed; the pulse is rapid, full, and bounding; headache may be intense; vomiting frequent; respiration hurried; the skin dry and burning; the thermometer mounting to 104°, 105°, 106°, or even higher.

Sweating stage.—After one or more hours of acute distress the patient breaks out into a profuse perspiration, the sweat literally running off him and saturating his clothes and bedding. With the appearance of diaphoresis the fever rapidly declines; headache, vomiting, thirst, and febrile distress giving place to a feeling of relief and tranquillity. By the time the sweating has ceased the patient may feel quite well; a little languid, perhaps, but able to go about his usual occupation. The bodily temperature is now often sub-normal, and may remain so until the approach of the next fit one, two, or three days later.

Duration of the fit.—The duration of an ague fit and of its constituent stages is very variable. On an average it may be put at six to ten hours, the

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cold stage occupying about an hour, the hot stage from three to four hours, the sweating stage from two to four hours.

The urine in ague.—During the cold stage the urine is often limpid and abundant, and is passed frequently; but during the hot and sweating stages it is scanty, loaded, sometimes albuminous. The amount of urea is increased, particularly during the cold stage; and so are the chlorides. The phosphates, on the contrary, diminished during the rigor and hot stages, are increased during defervescence. The augmentation in the excretion of urea commences several hours before the subjective symptoms of the attack begin, attains its maximum towards the end of rigor, and decreases during the hot and sweating stages, although still continuing above the normal standard. The excretion of carbonic acid follows a corresponding course. Dr. Sydney Ringer was the first to point out the interesting fact that, although the return of fever may be prevented by the administration of quinine, yet, for a time, a periodic increase in the excretion of urea occurs on the days on which the fever fit was due. The urine is often deeply coloured, giving with nitric acid the play of colour characteristic of bile pigment, or the brown colour described by Gübler as "hæmapheic." Glycosuria does occur, but is by no means common.

The spleen during the fit.—The spleen becomes enlarged to a greater or less extent during rigor. At first the swelling disappears in the interval, but it tends to become more or less of a chronic feature if the attacks recur frequently, more especially if they are associated with pronounced cachexia.

Period of the day at which ague commences.—Two-thirds of agues come off between midnight and midday. This is a fact to remember in diagnosis; especially when we have to face the possibility of recurrent pyrexial attacks being dependent on such conditions as liver abscess, tuberculosis, and septic states—conditions, be it remarked, in which febrile recurrence takes place almost invariably during the afternoon or evening.

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Atypical agues. — Cases are frequently met with in which all the above symptoms are very much toned down; in which, perhaps, a periodically recurring feeling of coldness, followed by languor, or a slight headache, or a slight rise of temperature, are the only symptoms indicating the presence of the malaria parasite in the blood. In some fevers, and these by no means the least dangerous, the subjective symptoms may at first be of so mild a character that the patient is able to go about his duties with a body-temperature of 103° or 104°; he may have no severe rigor, no headache, no severe gastric symptoms, no acute febrile distress of a disabling character. Some of the African fevers—so liable to assume suddenly a pernicious character—are of this nature. On the other hand, notwithstanding a comparatively slight rise of temperature, headache, prostration, or vomiting may be extremely distressing. There is an infinite variety in this respect. Evidently the toxin—if toxin there be—of the malaria parasites is far from being a simple body; probably, like tuberculin, it contains several ingredients arranged in different proportions in the several species and varieties of the parasite. Doubtless, also, the degree of infection, various combinations of the species of parasite, and individual idiosyncrasy play a part in determining the intensity and character of the reaction of the human body to the toxin.

Terms employed. — Acute malarial attacks which recur daily are called *quotidian ague;* if they recur every second day, they are called *tertian ague;* if every third day, they are called *quartan ague.* As a rule, the attacks tend to occur about the same time every day. In some cases the time of recurrence becomes earlier each day; such fevers are said to *anticipate.* Or they may occur at a later hour; in which case they are said to *postpone.* When the individual paroxysms are prolonged, so that one attack has not concluded before the next commences, the fever fits are said to be *subintrant.* When the fit is prolonged and periodicity is marked by only a slight fall of temperature, a slight sweating, a

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slight feeling of chilliness, the fever is said to *remit*—to be a *remittent*. Sometimes there is no remission; such a fever is said to be *continued*. It occasionally happens that two distinct pyrexial attacks come off the same day; such a fever is said to be *double*. All sorts of blendings of malignant infections, benign tertians, and quartans occur; in such the infection is said to be a *mixed infection*.

Relation of the phenomena of the fever fit to the stages of the parasite. — All the differences and peculiarities in the clinical phenomena of a malarial attack, complicated and hard to interpret in many cases though they be, are, it is believed, directly correlated to the phases of the intracorporeal life of the parasite; this organism is, in fact, the key to their interpretation. As already mentioned, as the time of rigor approaches, the pigment of the parasite, hitherto scattered throughout the substance of the little animal, becomes concentrated, and segmentation proceeds. Shortly before and during rigor, and as a direct cause of rigor, these segmented parasites are breaking up and, presumably, liberating their toxins. At the end of rigor, during the hot and during the sweating stages, the young parasites of the new generation—the small intracorpuscular bodies, and the leucocytes carrying the hæmozoin liberated at the breaking up of the segmented bodies—are in evidence, and the toxins liberated at the same time are being eliminated. During the interval the intracorpuscular parasites grow, become pigmented, and prepare for maturation. From the fact that parasites are present in the blood during apyrexia, and often in great abundance, it is evident that it is not the mere presence of the parasite in the blood corpuscle that causes the fever; most likely, as suggested, the pyrogenic agent is some toxin which is liberated and becomes free in the liquor sanguinis on the breaking up of the parasite. Consequently, we find that in remittent and continued types of malarial fevers segmenting parasites may be met with at all stages of the fever; and, conversely, that when parasites at all stages of development are

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met with, the associated fever is probably remittent, irregular, or more or less continued in type.

The foregoing are generalities which apply to all the types of malarial infection.

QUARTAN INFECTION

The parasite.—The parasite of quartan fever, *Plasmodium malariæ* (Fig. 19), has a cycle of seventy-two hours. At its earliest stages of epicorpuscular and of early unpigmented intracorpuscular life it takes the form of a small, roundish, clear speck (Plate I., Fig. 1, *a*), showing up somewhat distinctly against the hæmoglobin of the invaded corpuscle. At this stage, as contrasted with the other species of malaria parasites, it is further

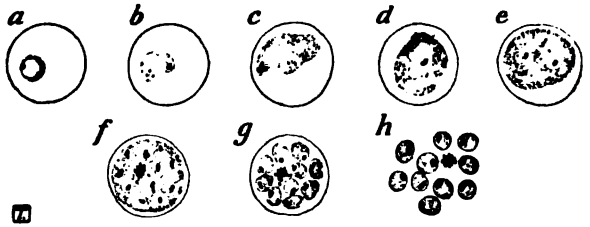

Fig. 19.—Quartan parasite: asexual stage: stained.

distinguished by the feebleness of its amœboid movement. Later, as soon as it becomes pigmented (Fig. 19, *b*, *c*, *d*, *e*, *f*), all amœboid movement ceases. (See also Plate I., Fig. 1, *b*, *c*, *d*, *e*, *f*.) Relatively to the other malaria parasites, the hæmozoin carried by the quartan is large in amount and coarse in grain, sometimes forming short rods. The segmented or mature parasite (Fig. 19, *g*, *h*) is made up of eight to ten elements arranged daisy-fashion and, usually, very symmetrically around the now centrally placed and massive block of very black hæmozoin. About the centre in each of the spherical or pear-shaped segments, which are slightly rough in outline, a shining nucleolus can usually be readily made out.

The gametocyte, or sexual form, is a spherical

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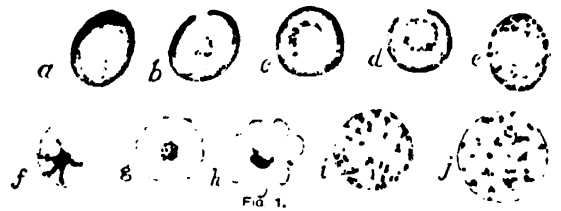

Fig 1.

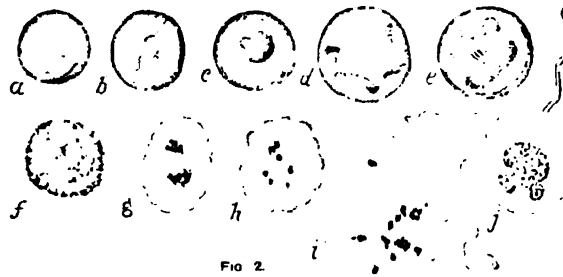

Fig 2.

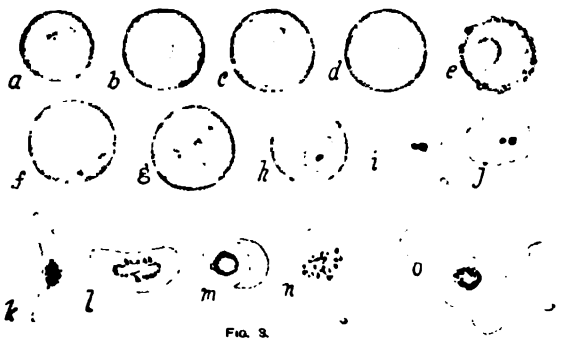

Fig. 3.

PLATE I.—Malaria Parasites.

Fig. 1.—Parasite of quartan infection. Fig. 2.—Parasite of benign tertian infection. Fig. 3.—Parasite of sub-tertian infection ("æstivo-autumnal"). (*Compiled from Thayer and Hewetson.*)

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pigmented body looking like an ordinary large intracorpuscular pigmented parasite (Plate I., Fig. 1, *i*) that has escaped from the red corpuscle in which it had developed. It may be recognised sometimes by the very active movement of the hæmozoin granules. This phase, rarely seen, occurs almost exclusively during the pyrexial stage of the cycle. Further, the quartan parasite does not, as does that next to be described—the tertian parasite, cause marked enlargement of the blood corpuscle in which it lies. When mature it completely fills the normal-sized corpuscle, scarcely a rim of hæmoglobin being visible (Fig. 19, *f*); so that it sometimes looks at this stage as if it were a free and independent body floating about in the liquor sanguinis.* All quartan parasites do not proceed to segmentation, or to gamete formation; some are said to degenerate into the peculiar clear, dropsical-looking spheres, filled with dancing particles (Plate I., Fig. 1, *i*), which form a striking feature in certain malarial bloods. A considerable proportion of these free, dropsical-looking bodies with active hæmozoin are probably male gametocytes which, after being placed on the microscope slide, and after escaping from corpuscles, have failed to project their microgamete filaments; others, doubtless, are granular female gametes. The failure to project microgametes, in many instances, is probably not normal, but an effect of mechanical disturbance from pressure of the cover-glass, or of other circumstances inherent in the artificial conditions under which we necessarily observe these bodies. In more normal conditions the emission of microgametes may be more frequently effected.

The "daisy"—as it is sometimes called—or segmented phase of the quartan parasite, is more frequently seen in the peripheral blood than is the corresponding phase of the other malarial parasites. For this reason, and because of the easy visibility of

* In malarial blood the corpuscles are apt to vary in size, as in other anæmic conditions. A quartan parasite in a megalocyte may therefore simulate a tertian. Usually the including blood corpuscle is, or seems, smaller than normal.

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the parasite at all its stages owing to its size and to the large amount of hæmozoin it carries, and because the entire intracorporeal cycle is completed in the peripheral blood, the quartan is the best form of malaria parasite for the beginner to study.

Geographical distribution.—The fever which the quartan parasite gives rise to—single, double, or treble quartan ague—is, relatively, much more common in temperate latitudes than in the tropics. Formerly it was common enough in England; it is still far from rare in the malarious districts of north and mid-Europe and, doubtless, elsewhere under similar climatic and telluric conditions. But, as we proceed south, it becomes, relatively to the other forms of malaria, rarer. In the tropics in some highly malarious places it is unknown. Thus in a paper read at the Calcutta Medical Congress of 1894 Crombie mentioned that in his large experience he had rarely seen quartan ague. As his experience applied particularly to Calcutta and its environs, it may not hold for the whole country; in fact, Ross and others state that the quartan parasite is common enough in Madras and elsewhere in India. I have seen it in blood films from Mauritius; Ross mentions it as occurring in Sierra Leone. Doubtless it occurs in limited districts throughout the tropics. Thus, though relatively rare in many of the West India Islands, it is a common form, according to Freeman, in Antigua. The general statements that quartan ague is, relatively to the other forms of malaria, more a disease of the temperate zones than of the tropics, and, further, that both in the tropical and temperate zones it has topographically a very limited distribution, probably express the truth.

The fever.—The ague fit in quartan is generally smart while it lasts, and well defined as regards its constituent stages (Fig. 20). It does not tend so markedly, as is the case with the other malarial infections, to the rapid development of cachexia. Although the individual attacks are very amenable to quinine, the infection appears to be of a more persistent nature than that of tertian and sub-tertian

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malaria; attacks, therefore, are prone to recur during several years.

TERTIAN INFECTION

The parasite.—The early stage of the benign tertian parasite, *Plasmodium vivax* (Plate I., Fig. 2), resembles that of the quartan inasmuch as it consists of a small pale speck on, or in, the invaded red blood

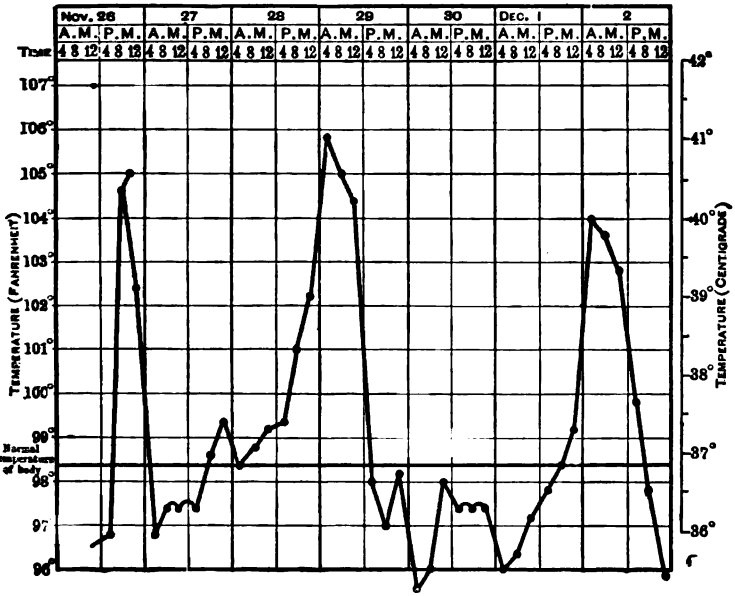

Fig. 20.—Chart of quartan ague.

corpuscle (Plate I., Fig. 2, *a*); it differs in exhibiting very much greater amœboid activity, changing its form and location in the corpuscle incessantly, besides pushing out and retracting pseudopodia (Plate I., Fig. 2, *b*). This amœboid activity persists during growth and the formation of hæmozoin, though in a progressively diminishing degree; it gives rise to great and rapidly changing irregularities in the contour of the parasite (Plate I., Fig. 2, *c*, *d*, *e*), but is almost entirely

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suspended by the time hæmozoin-concentration is effected. In the tertian parasite the hæmozoin particles are, on the whole, finer than those of the quartan parasite; and, moreover, are in a state of much more active and incessant movement, constantly changing their position in the peripheral region in which they, for the most part, seem to lie (Plate I., Fig. 2, *f*). Another, and highly characteristic, accompaniment of tertian infection is the considerable hypertrophy and marked decolorisation of the corpuscles containing the parasite (Plate I., Fig. 2, *d*, *e*, *f*, *g*). Sometimes the affected corpuscles seem nearly twice the diameter of the healthy ones; and nearly always, if the parasite is of any magnitude, the rim of hæmoglobin has a "washed-out" look, sometimes being almost colourless.

In corpuscles invaded by the tertian parasite, deep coloration with Leishman's or Giemsa's stains brings out a feature which does not occur in those attacked by quartan or sub-tertian parasites. With these stains in tertian invaded corpuscles the hæmoglobin is speckled with chromophilic particles called "Schüffner's dots." This is a feature of some diagnostic value. In the very young phases of the parasite it is not always present; unfortunately for its diagnostic value, these are just the phases that are difficult to diagnose from quartans and sub-tertians.

In the tertian parasite, when segmentation is completed, the resulting body, instead of the very symmetrical, daisy-like figure of the quartan, resembles rather a cluster of grapes in some more or less central part of which one or two masses of dark pigment have accumulated among the berries (Plate I., Fig. 2, *h*; also Figs. 1 and 2, *b*). The little spherules forming the cluster—fifteen to twenty-six in number—are smaller, smoother, and more spherical than those of the quartan parasite; seldom, in the unstained condition, exhibiting their nucleoli. I believe that in natural, uncompressed conditions the tertian "rosette," as it is called, tends to pass from the disc form, impressed on it originally by the shape of the corpuscle, to something more approaching a globular form.

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In the tertian, as in the quartan parasite, the gametocyte is a spherical body resembling closely the mature parasite from which the segmented body is evolved (Plate I., Fig. 2, *j*). It is seen more particularly, just as in the case of the quartan infection, after and not unfrequently about the time of rigor. The tertian gametocyte is considerably larger than that of the quartan and sub-tertian parasite.

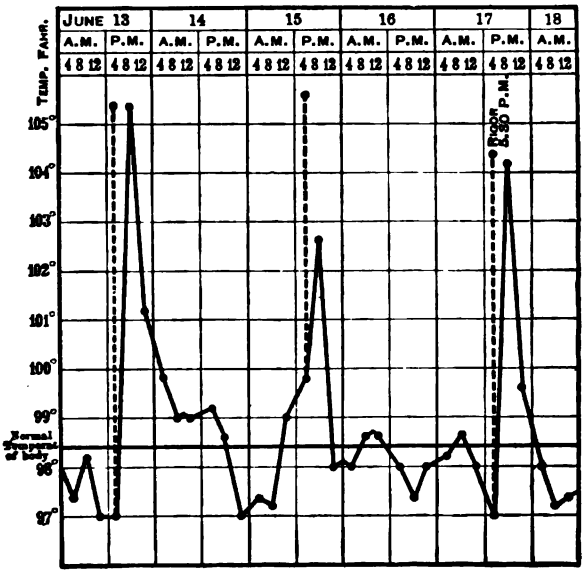

Fig. 21.—Chart of benign tertian ague.

Geographical distribution.—The tertian parasite, probably the commonest form of malaria parasite, occurs in temperate and tropical latitudes alike. It is often found as a double infection, and is, perhaps, the most frequent cause of quotidian as well as of tertian agues.

The fever.—The fever it gives rise to, except in the matter of the spacing, which is one of forty-eight hours, resembles that caused by the quartan parasite (Fig. 21).

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MALIGNANT INFECTIONS

Many authorities refuse to recognise more than one species of crescent-forming parasite. On the other hand, carefully conducted observations, both microscopical and clinical, seem to indicate a plurality of species. I shall follow the latter view.

The three parasites (Plate I., Fig. 3, and Plate II., Fig. 1) described by the Italian pathologists in connection with malignant malarial infection, although often associated together as well as with the benign parasites, are each of them occasionally found in what may be termed pure culture. From a study of such cases the morphological and distinguishing characters of the different species, and their special pathological effects, have been more or less satisfactorily made out. Although much remains to be done, enough is already known to enable us, in a measure, to differentiate them from each other as well as from the benign parasites, and to justify their being placed in a group by themselves.

Characters possessed in common by the malignant parasites. — One notable feature in regard to them is that they are very much smaller than the benign parasites. The earlier unpigmented phase, owing partly to minuteness, partly to its forming but a thin and very transparent object in the hæmoglobin, is hard to see. When first mounted on the slide the amœboid movements are very active (Plate I., Fig. 3, *d*). In a short time these subside somewhat, and then the little parasites tend to assume a more passive condition and to arrange themselves as tiny, though very definite and easily recognised, rather bright, colourless rings (Plate I., Fig. 3, *a*, *b*, *c*, *e*). Sometimes these rings may revert to the amœboid condition, and this, perhaps, for several times in succession; ultimately the ring form becomes permanent. Multiple infection of individual corpuscles (Plate I., Fig. 3, *g*) is often encountered, and this much more frequently than in the benign infections; doubtless, this is owing to the prodigious number of parasites present in some malignant infections. As development advances, the

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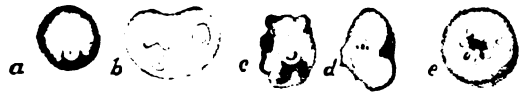
FIG. 1.



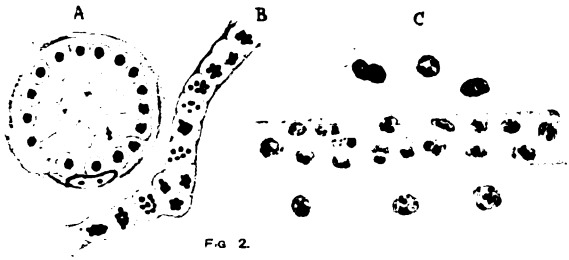


FIG 2.

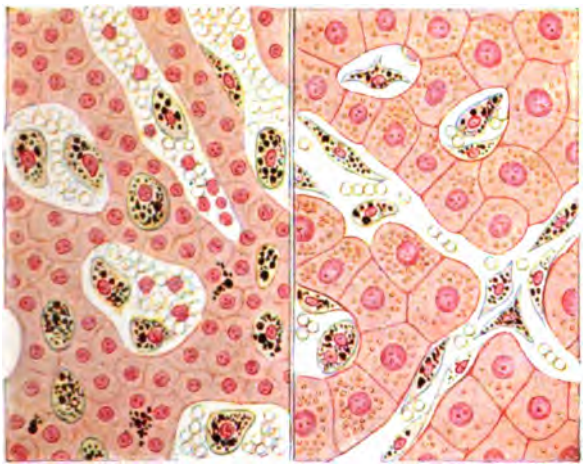


FIG 3 FIG 4.

PLATE II.—MALARIA PARASITES.

Fig. 1.—Parasites of the pigmented malignant quotidian (*Marchiafava and Bignami*). Fig. 2.—Brain capillaries containing malaria parasites. A, transverse section; the blood corpuscles at periphery invaded by unpigmented parasites; B, vessel filled with sporulating unpigmented parasites; C, blood corpuscles in capillary, and others free in the brain substance, each containing small pigmented parasites (*Mannaberg*). Fig. 3.—Pernicious malaria (spleen). Fig. 4.—Pernicious malaria (liver). (*Kelsch and Kiener.*)

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invaded corpuscles seem to be filtered out by the capillaries and small arteries (Plate II., Fig. 2, A, B, C) of the deeper viscera and of the bone marrow. So that even in severe infections the later pigmented stages are by no means proportionately represented by, or even frequently encountered in, finger blood; the segmenting form (Plate I., Fig. 3, *i*, *j*) still less so. To find numerous examples of the more advanced stages of these parasites it is necessary to aspirate splenic blood, or to search in fatal cases in the deeper viscera, or in the bone marrow immediately after death. Owing to this absence of the more advanced forms from the peripheral circulation, the duration of the life-span of these parasites is difficult to fix; probably it varies between twenty-four and forty-eight hours, being not very constant even in the same type.

"Brassy bodies." — Malignant parasites frequently lead to a peculiar shrivelling of the invaded corpuscles, many of which, in consequence, are small, crenated, or folded, and very dark. This dark, irregularly shaped corpuscle the Italians, from its colour, have designated "brassy body" (Plate I., Fig. 3, *e*). In the interior of these dark, shrivelled corpuscles the parasite can generally be made out as a minute pale ring.

The crescent body characteristic.— Most distinctive feature of all, the malignant parasites—at all events the sub-tertian—form crescent gametocytes.

Time when crescents appear; not a fever form.—It has been already remarked that these crescent bodies are not to be seen at the very commencement of an infection. A week usually elapses between the first appearance in the peripheral blood of the small intracorpuscular parasites and the first appearance of the crescent bodies.* Once the latter begin to appear

* There has been a good deal of speculation as to why certain parasites develop into schizonts, whilst others become gametocytes. The circumstance of the late appearance of the gamete is looked upon by some as evidence that the blood, from repeated development in it of swarms of endogenous parasites, has become exhausted as a pabulum, and that in consequence of this the parasite is directed to a line of development providing for life and growth elsewhere, that is in the mosquito. The analogy of other sporozoa and of the bacteria supports this view.

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they generally tend to increase in number during a few days. They may persist, though after a time in decreasing numbers, in the circulation for one, two, three or even six weeks after the small fever-causing intracorpuscular parasites and their associated fever have disappeared, whether spontaneously or in consequence of the administration of quinine. Although when given early in an infection quinine may prevent the appearance of crescents, yet, when they are once formed, the drug has apparently no influence on these bodies nor on their capacity for emitting microgametes. The crescent body does not cause fever. Its presence is usually associated with marked cachexia.

It is a singular fact that in many of the worst types of tropical malaria—as that of tropical Africa—crescents are few in number, and in some instances cannot by ordinary examination be found. A. Plehn states that during a period of two years in Africa he only once saw the flagellated body. On the other hand, when we meet with these African infections in England, crescents are frequently encountered, and often in great abundance; at all events, this is my experience.

Characters of the fever.—It is found that the fevers produced by the malignant parasites are apt to be very irregular in their course. The rigor stage is relatively less marked; the pyrexial stage is more prolonged, and is often characterised by a tendency to adynamic conditions, together with vomiting, intestinal catarrh, pains in the limbs, anorexia, severe headache, and depression. After apparent recovery from the fever there is a great proneness to relapse at more or less definite intervals of from eight to fourteen days. Such fevers are accompanied by rapid destruction of corpuscles, and are usually followed by marked cachexia. At any time in their course symptoms of the gravest character may declare themselves.

QUOTIDIAN INFECTIONS

The quotidian infections are comparatively rare; at all events, they have not been very frequently

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recognised or adequately described. Many regard them as but varieties of the common sub-tertian infection.

The parasite.—The parasites are said to be of two kinds (very generally in association), the pigmented, *Laverania præcox* (Plate II., Fig. 1), and the unpigmented, *Laverania immaculata.* In both the cycle is approximately one of twenty-four hours; in both the young parasites exhibit very active movements, and tend to assume the ring form. Before segmentation they grow so as to occupy from one-fifth to one-third only of the corpuscle. Both form little heaps of from six to eight very minute spores.

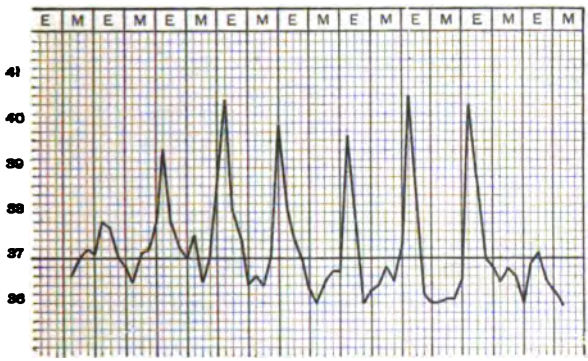

Fig. 22.—Chart of quotidian infection.

In the unpigmented parasite hæmozoin is never seen unless it be in the crescent phase—a phase the occurrence of which has not been satisfactorily established; in this phase, however, hæmozoin is never absent. In the pigmented parasite there is a considerable amount of fine hæmozoin, which at the segmenting stage—rarely seen in peripheral blood—collects in the usual way into one or two more or less central clumps.

The fever.—The fever is such as just described, a typhoid-like depression being generally a prominent feature in well-marked cases (Fig. 22).

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SUB-TERTIAN INFECTION.

The parasite.—*Laverania malariæ*, the usual parasite (Fig. 23) of malignant infection, is, in many respects, like that of ordinary tertian, only smaller, attaining when mature from a half to two-thirds the size of the corpuscle it occupies. The infected blood-corpuscle may be altered in colour in the direction of being either darker or lighter; sometimes it shrinks, or it may become a "brassy body." The segments of the rarely encountered mature segmenting parasite number usually ten or twelve, and are arranged along with the associated clump or clumps of hæmozoin in an irregular heap. The crescent-shaped gametocyte is a characteristic feature.

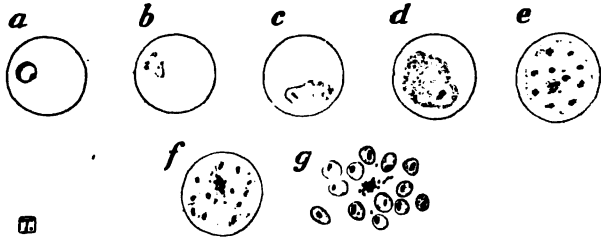

Fig. 23.—Evolution of the sub-tertian parasite: asexual cycle.

The fever.—The associated symptoms are, in many respects, very different from those caused by the tertian parasite. In the first place, though rigor is not so marked, the hot stage lasts longer—often exceeding twenty-four hours; in fact, the tendency for the successive paroxysms to overlap, to become subintrant, is very marked. Moreover, where the intermissions are distinct, as Marchiafava and Bignami point out, the crisis is generally unlike that of ordinary tertian. There is frequently what is called a double crisis; that is to say, when the fever has attained its apparent fastigium there is a drop of one or more degrees of temperature—the "false crisis," to be followed by a fresh rise, which is then followed by the "true crisis." This peculiar phenomenon the

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writers referred to attribute to the presence of two swarms of parasites, one of which matures somewhat later than the other. (Fig. 24.)

The tendency to the development of pernicious symptoms, to the production of cachexia, and to relapse is similar to what appears to be the case in malignant quotidian infections.

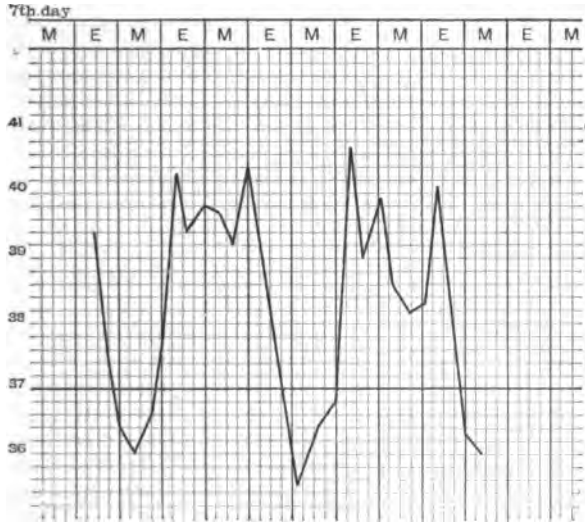

Fig. 24.—Chart of sub-tertian infection.

Geographical distribution.—All these malignant parasites are confined to the warmer regions of the earth, and to the more intensely malarial districts in these; hence the name "tropical" which has been applied to this type of infection. In the sub-tropical zones they occur as first infections only in late summer or early autumn; hence the name "æstivo-autumnal."

Microscopical examinations in malignant fevers.—In malignant infections the pigmented phase of the fever-causing forms of the parasite is not very frequently met with in peripheral blood. When found,

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and especially when it is observed that the pigment has become concentrated, it is a sure indication that a paroxysm is impending. On the occurrence of chilliness or of rigor, and at least during the earlier stages of the paroxysm, many small unpigmented parasites, sometimes exhibiting active amœboid movement, sometimes appearing as rings, will be found in finger blood; but towards the end of fever these unpigmented forms often diminish in number, and all evidence of parasitic infection may even disappear from the blood till the approach or incidence of the next paroxysm. Of course crescents and pigmented leucocytes may be found during these temporary absences of the intracorpuscular parasites. The segmenting forms of the malignant parasite are best found by aspirating the spleen with a hypodermic needle—hardly a justifiable procedure unless in exceptional circumstances.

CLINICAL FORMS OF BENIGN AND PERNICIOUS MALARIAL FEVERS

General statements.—The foregoing account, so far as it goes, and so far as it relates to the clinical manifestations produced by uncomplicated and typical infections, is true enough. But, as there may be an infinite variety as regards the number of the parasites present, individual susceptibility, concurrence of several species (mixed infection being far from uncommon), or of several generations of the same species of parasite maturing at different times, there may be a corresponding variety in the clinical manifestations.

In more temperate climates, and in the winter and spring seasons of warmer latitudes, malarial fevers are usually distinct intermittents. Fresh infections occurring in these places and seasons, so far as the subject has been studied, are found to be produced by the tertian and quartan parasites, and are, therefore, of little danger. Relapses, however, of malignant infections, originally contracted during the hot weather, may occur during the cold season—in fact, are far from uncommon then.

First attacks, though produced by one of the benign parasites, may assume the characters of a

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remittent; generally, in temperate latitudes, they are frank intermittents. First attacks of malignant malaria, although they may in a few instances be intermittent, are in the majority of cases remittent in type. So are the attacks resulting from extensive reinforcement by fresh parasites (through fresh infection) of the old stock which a fever subject may carry about him in a latent condition. The first attack experienced by a new comer to a highly malarious district with a hot climate is, therefore, generally remittent and severe.

It is neither necessary, nor desirable, to attempt to describe in detail the infinite variety malarial attacks exhibit. It would be impossible in a limited space to do so; and, if done, the result would amount only to an uninteresting and unprofitable ringing of the changes on rigor, pyrexia, diaphoresis, bilious vomiting, bilious diarrhœa, constipation, catarrhal gastritis, headache, bone-ache, prostration and so forth. The picture would be further confused by the fact that the natural procession of events is generally, nowadays, disturbed by the action of quinine, the use of which is almost universal with Europeans in the tropics; so that it is difficult to say how any given malarial fever would develop, or how it would terminate, if untreated. Sometimes in the case of natives of tropical countries, who may not always command a few grains of quinine, such fevers pass into a typhoid state, with dry brown tongue, sordes in the mouth, and muttering delirium, and may end in collapse and death. In others, untreated remittents and intermittents gradually subside spontaneously in the course of a week or fortnight; or the remittent may merge into an intermittent which, in the course of weeks or months, subsides for a time, to recur every now and again at longer or shorter intervals. These recurrences may take place at fairly definite intervals; "long-interval fevers" the Italians have named them. Kelsch and Kiener allowed certain remittents in Europeans to run their course unchecked by quinine; they found that in ten or twelve days the fever gradually expended itself. Under favourable hygienic conditions the parasite

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and the associated fever frequently disappear together spontaneously. Occasionally the fever forms of the parasite may be present in the blood for days on end without causing acute clinical symptoms.

REMITTENT TYPES.

Bilious remittent.—One type of fever, known as bilious remittent, has long been recognised on account of the bilious vomiting, gastric distress, sometimes bilious diarrhœa, sometimes constipation, which accompany the recurring exacerbations. It is further distinguished by the pronounced icteric or, rather, reddish yellow or saffron tint of skin and scleræ; a tint derived, probably, not from absorption of bile as in obstructive jaundice, but from modified hæmoglobin (hæmaphein) free in the blood or deposited in the derma and sclerotia. These bilious remittents are very common in the more highly malarious districts of Africa, America, the West Indies, India, and, in fact, in all malarious tropical countries. They are not specially, nor directly dangerous in themselves, but they result usually in profound anæmia, and are often but the prelude to chronic malarial saturation, bad health and invaliding.

Typhoid remittent.—A modification of the bilious remittent — what Kelsch and Kiener call "typhoid remittent"—is very much more grave as affecting life than the simple bilious remittent. In the typhoid remittent, typhoid symptoms—such as low delirium, prostration, dry tongue, swelling of spleen and liver, subsultus tendinum, marked melanæmia—are superadded to the usual symptoms. Though recovery is the rule, a considerable proportion of such attacks prove fatal.

Adynamic remittent.—The same writers class by themselves a set of cases they call "adynamic remittent"; cases which are characterised by fatuousness, restlessness, nervous depression, intense muscular and cardiac debility, profound and rapid blood deterioration, icterus, leucocytosis, melanæmia, liability to syncope, occasionally hæmoglobinuria, liability to hæmorrhages, and a marked tendency to local gangrene.

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Tuberculosis, syphilis, renal disease, or alcoholism will often be found as factors in determining the two latter types of fever.

PERNICIOUS ATTACKS.

Many writers have drawn attention to what are called pernicious attacks or pernicious symptoms—the French neatly designate them "accès pernicieux"—a series of phenomena, the possibility of the appearance of which, not only in the course of remittents, but in the course of what is seemingly only an ordinary paroxysm of intermittent fever, should never be lost sight of by the practitioner in tropical climates. These "accès pernicieux" may supervene in apparently mild cases and carry off the patient with horrifying suddenness—as suddenly as an attack of malignant cholera. The wary practitioner is always on the look-out for them, and is always prepared with measures to meet them promptly when they threaten.

Pernicious attacks are roughly classified into cerebral and algide. The cerebral are divisible into hyperpyrexial, comatose, convulsive, paretic, and so forth; the algide into syncopal, choleriform, dysenteric, hæmorrhagic, etc.

Cerebral Forms.

Hyperpyrexial.—There can be little doubt that many of the cases of sudden death from hyperpyrexia and coma, usually credited to what has been called "ardent fever" or "heat apoplexy," are really malarial. If careful inquiry be made into the antecedents of many of these cases, a history of mild intermittent will often be elicited; or it will be found that the patient had been living in some highly malarious locality.

In the course of what seemed to be an ordinary malarial attack the body temperature, instead of stopping at 104° or 105° Fahr., may continue to rise and, passing 107°, rapidly mount to 110° or even to 112°. The patient after a brief stage of wild maniacal or, perhaps, muttering delirium, becomes rapidly unconscious, then comatose, and dies within

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a few hours, or perhaps within an hour, of the onset of the pernicious symptoms.

Comatose.—Or the patient, without hyperpyrexia, the thermometer perhaps not rising above 104°, or even lower, may lapse into coma. The coma may pass away with crisis of sweating; on the other hand, an asthenic condition may set in and death from collapse supervene.

Other cerebral forms.—Besides these hyperpyretic and comatose conditions, other forms of cerebral attack may occur in the course of malarial fevers. Thus there may be *sudden delirium* ending in coma and, perhaps, death; *convulsive seizures* of an epileptic or of a tetanic character, with or without delirium or coma—forms especially common in children; various forms of *apoplectic*-like conditions and of *paralysis*, complicated it may be with *aphasia*. Seizures of this description, if not fatal, may eventuate in *permanent psychical disturbances*. Temporary debility, or even complete *loss of memory* may succeed severe malarial infection.

Embolism of cerebral capillaries.—These cerebral attacks are now explained, and it appears to me correctly explained, by the supposition, founded on actual *post-mortem* observation, that they depend on embolism by the malaria parasite of the capillaries of the various nerve centres (Plate II., Fig. 2) involved; in hyperpyrexia, the thermic centres; in aphasia, Broca's convolution; and so on. By microscopical examination of properly prepared sections of the brain in fatal cases, such a plugging of the vessels can generally be readily observed. The earlier students of malarial melanæmia had remarked the presence of hæmozoin in the cerebral capillaries in many cases of this description, and, overlooking the including parasite, attributed the associated symptoms to thrombosis by the hæmozoin.

Malarial amblyopia.—In rare instances a comatose pernicious attack eventuates in blindness. The amblyopia is usually transient, lasting for an hour or two only. On the other hand, it may be persistent; in which case, according to Poncet, optic

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neuritis, peripapillary œdema, extravasation of leucocytes, plugging of retinal and choroidal vessels by parasites or pigmented leucocytes, and consequent multiple hæmorrhages, may be found in the fundus. If the hæmorrhages are minute, they are discoverable by the microscope only. These fundus changes differ from those in quinine amblyopia. In the latter, depending on retinal anæmia from toxic spasm of the arterioles, the amblyopia is more persistent; the discs are white and the vessels shrunken; there are no inflammatory symptoms; and central vision is the first to recover. (See the table on page 74.)

Algide Forms.

The algide forms of pernicious attack, as indicated by the name, are characterised by collapse, extreme coldness of the surface of the body, and a tendency to fatal syncope. These symptoms usually coexist with elevated axillary and rectal temperature.

Gastric form.—This may be associated with, and in a measure be dependent on, acute catarrhal dyspeptic trouble. It is accompanied by severe epigastric distress, tender retracted abdomen, and incessant vomiting. The vomited matter may contain blood.

Choleraic form.—Malarial attacks are sometimes accompanied by choleraic symptoms. The stools suddenly become loose, profuse, and numerous. They are not generally so profuse or colourless as the rice-water discharge which pours from the patient in true cholera; they retain a certain amount of biliary colouring, and may be mucoid or even bloody. As in cholera, the serous drain may lead to cramps in the limbs, loss of voice, pinched features, washer-woman's fingers, almost complete suppression of urine, and, perhaps, to fatal collapse. Such attacks are very deceptive, and may be mistaken for true cholera. The high axillary temperature, if present; a history perhaps of recent ague fits; the subsequent rapid disappearance of choleraic symptoms on the appearance of the hot and sweating stages; the colour of the stools, and other collateral circumstances,

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TABLE OF DIAGNOSTIC POINTS IN QUININE AND MALARIAL AMBLYOPIA.

QUININE AMBLYOPIA.	MALARIAL AMBLYOPIA.
History.—Quinine taken in large doses, not less than thirty grains.	*History.*—Quinine may have been taken, but not necessarily in large doses.
Onset.—Sudden, accompanied by deafness; both eyes are affected.	*Onset.*—Not usually sudden, but it may be so if hæmorrhage has occurred in the macular region. There is no deafness, and both eyes are not necessarily affected.
Pupils.—Widely dilated, and whilst loss of vision continues they do not react to light.	*Pupils.*—React to light.
Vision.—Completely lost for a time.	*Vision.*—Never completely lost.
Ophthalmoscopic appearances.—A white haze over fundus; cherry-red spot at macula; optic disc pale; retinal vessels markedly constricted.	*Ophthalmoscopic appearances.*—There is optic neuritis; optic disc is of characteristic greyish red colour; retinal hæmorrhages, and sometimes vitreous opacities.
Termination.—Usually some permanent defect in the field of vision or in colour vision. Central vision recovers first; optic disc is unusually white, and retinal vessels small.	*Termination.*—Some cases recover completely; in others greater or less permanent defect of vision remains.
Treatment.—Stop quinine. Amyl nitrite has been recommended to induce dilatation of retinal vessels.	*Treatment.*—Give quinine.

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usually suffice for diagnosis, particularly if they are supplemented by a microscopical examination of the blood. Although not usual, recurrence of the choleraic symptoms may take place at the next fever period. A dangerous type of malarial fever prevalent in the Punjab is often ushered in by such symptoms; without the microscope its true nature may be hard to recognise.

Dysenteric and hæmorrhagic forms.—Another form of pernicious attack is characterised by the sudden appearance of dysenteric symptoms; yet another by severe and recurring hæmatemesis, or by hæmorrhage from the bowel or elsewhere. The possibility of a suddenly developed dysentery being of malarial origin must therefore be kept in view; particularly if in what appears to be ordinary dysentery axillary temperature is found to be abnormally high. In every case of dysentery of this kind, or of hæmorrhage from stomach or bowel, in a patient who has recently been exposed to the chance of malarial infection, the possibility of the symptoms being an expression of malarial disease must never be overlooked; an examination of the blood must be made in all such cases before treatment is instituted.

Syncopal form.—In the preceding types of algide pernicious malarial attack the dangerous symptoms mostly show themselves in the rigor stage of the fever. There is yet another form in which the danger appears to depend on an exaggeration of the symptom usually hailed as bringing relief and, for the time, freedom from danger. Thus the sweating of the stage of defervescence may be excessive and cause collapse, which, if the patient rise up suddenly or make an undue effort, may lead to fatal syncope. Weak and cachectic patients, therefore, should be warned of this possibility, and not be permitted to rise suddenly, or to exert themselves in any way during the defervescence of an ague.

The *pathology* of these various forms of algidity is in all likelihood of a very mixed character. In the gastric,

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TABULAR STATEMENT OF THE CHARACTER-

Modified from

	Duration of Development.	Movement.	Hæmozoin.	Maximum Size.	Form of Segmentation
1. Quartan parasite, *Plasmodium malariæ.*	72 hours	Slight movement in the immature forms	Coarse grains; little or no movement	The size of a red blood corpuscle	Daisy form; the single spores roughish, with distinct nucleolus
2. Tertian parasite, *Plasmodium vivax.*	48 hours; or less in anticipating types	Active amœboid movement in the immature and also in the middle-aged forms	Finer granules in immature forms; often in the larger actively swarming	Size of a red blood corpuscle; sometimes even larger	Sunflower or grape-like; single spores small, round; nucleolus rarely seen
3. Pigmented quotidian parasite, *Laverania præcox.*	24 hours	In the unpigmented immature stage very actively amœboid; less active when hæmozoin accumulates	Very fine; later coalesces in one or two clumps; does not swarm	½–¾ the size of a red blood corpuscle	Irregularly formed heap
4. Unpigmented quotidian parasite, *Laverania immaculata.*	24 hours or less	Very active amœboid movement	None	½–¾ the size of a red blood corpuscle	Star-shaped, or in irregular heaps
5. Sub-tertian parasite, *Laverania malariæ*	48 hours or less.	Active; the movement remains present in the pigmented stage	Fine; often shows oscillatory movement	½–¾ the size of a red blood corpuscle	Irregular heaps

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ISTICS OF THE VARIOUS MALARIA PARASITES.

Mannaberg.

Number of Merozoites.	Form of Gametocyte.	Alterations in the Infected Blood Corpuscles.	Relative Number of Parasites seen in Peripheral and Visceral Blood respectively.	Influence of Quinine.	Liability to Reappearance of Parasite after leaving Infective Regions.
6–12	A sphere	The red blood corpuscles are little discoloured, and are not materially altered in size; some appear smaller.	Parasites seen in peripheral circulation throughout the whole cycle, and in as great numbers as in visceral blood	Causes disappearance of parasite readily	Liability persists for a very long period
15–20 (often less)	A sphere	The red blood corpuscles are often hypertrophied, and lose colour, it may be completely. Schüffner's dots in deeply stained specimens.	Parasites seen in peripheral blood throughout the whole cycle, but not in such large numbers as in visceral blood	Causes disappearance of parasite readily	Liability persists for long period
6–8 (even more)	A crescent (?)	The red blood corpuscles shrink often, and are then either darker-stained (copper colour) or may be completely decolorised	An enormously greater number of parasites present in internal organs as compared with peripheral blood. The latter part of the cycle takes place in internal organs only	Causes disappearance of parasite less readily	After a few months less liability to recurrence
6–8	A crescent (?)	The red blood corpuscles shrink frequently, and are dark	Ditto	Ditto	Ditto
10–12, rarely 15–16	A crescent	The red blood corpuscles shrink frequently; they are dark, or may be perfectly colourless	Ditto	Ditto	Ditto

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choleraic, hæmorrhagic and dysenteric types there is probably an accumulation of parasites in the vessels of the intestinal mucosa; such accumulations of parasites have been described. In those attacks in which profuse sweating is the dangerous element, the diaphoresis may be regarded, at all events in part, as symptomatic of excessive blood destruction—of what is, in reality, equivalent to a sudden and extensive hæmorrhage; or it may be that it is only an excessive reaction to the malarial toxin. The dangerous syncope attending all types of algidity is secondary, and merely an expression of collapse.

A phenomenon occasionally observed in pernicious attacks, especially in those of an algide type, is the flooding of the peripheral blood with vast numbers of parasites, it may be at all stages of development—gametes both mature and immature, as well as schizonts at all stages of development. The prognosis in such cases is bad.

A practical experience of these suddenly developed pernicious fevers of the tropics teaches that we should never make light of any malarial attack; particularly if it be of a mild irregular character and imperfectly controlled by quinine, and if small parasites, or the crescent form, be present. The practitioner should be on the alert for any danger signal—mental aberration, restlessness, tremor, peculiarity in behaviour, alteration in knee reflexes, and other indications of grave implication of the nervous system. It further teaches that the subjects of such fevers should be particularly careful to guard against chills, fatigue, insufficient and unwholesome food, and all causes of physiological depression.

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CHAPTER IV

MALARIA: MORBID ANATOMY AND PATHOLOGY

The blood in malaria.—As the malaria parasite is a blood parasite, we naturally expect that the primary effect of its presence will be exercised on, and manifested in, the blood; and as the parasite lives in and at the expense of the corpuscles, destroying a certain proportion of them—in fact, all those attacked—we look, in the first instance, for a corresponding diminution in the number of the corpuscles—an oligocythæmia.

Oligocythæmia.—Accordingly, when in malarial disease we come to measure accurately the corpuscular richness of the blood, we do find a decided oligocythæmia; and, not only this, but we find a degree of oligocythæmia greatly in excess of anything we might expect, or which can be accounted for by, or is in correspondence with, the proportion of corpuscles attacked and directly consumed by the parasite, judging by what we see in finger blood—peripheral blood. If, for example, every hundredth corpuscle contains a parasite we might look for something like a quotidian, tertian, or quartan 1 per cent. reduction in the total number of blood corpuscles; if every twentieth corpuscle contains a parasite—a very high and unusual proportion—we might look for a similarly timed 5 per cent. reduction.

Now this is an amount of hæmolysis which should be easily compensated by the latent physiological hæmogenetic margin, and which one would not expect to show as a definite anæmia, or to show only after the recurring drain had been kept up for some considerable time. But what are the clinical facts? One or two paroxysms only, of some malarial fevers, may be immediately followed by an

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anæmia so pronounced as to be discernible to the eye in the intense pallor of the skin and visible mucous surfaces. On counting the corpuscles in such a case we note a regular drop in their number of from 5 to 10 per cent. per paroxysm. Often, after a single paroxysm of some pernicious fever, as many as half a million, or even one million, corpuscles per c.mm. drop out of the normal five millions; and this reduction may go on, as paroxysm follows paroxysm, until the corpuscular richness has fallen to one million, or even less.

Diminished hæmoglobin value of corpuscles.—Not only is there in many, in fact in most, cases of malarial disease a pronounced oligocythæmia, but there is, in addition, a marked diminution in the hæmoglobin value of the surviving corpuscles; it may fall 10, 20, or even as much as 50 per cent.

Diminished amount of blood.—And not only is there this marked diminution in the proportion of the corpuscles to the bulk of the blood and in their hæmoglobin value, but there is, furthermore, in all malarial conditions of any considerable standing, a marked diminution in the volume of blood. Thus it comes that at the *post-mortem* examination of such a case we do not always meet with that congestion of the organs which is so usual a feature in most specific fevers. On the contrary, although in quite recent cases visceral congestion may be marked enough, if a malarial fever has been of any considerable duration, the venous system, with the exception of that appertaining to the spleen, liver, and portal system generally, may be markedly empty. And thus it is that often, when we would make a preparation of blood from the living malarial patient, we may find that not only is the blood thin and watery, but that it does not flow freely from the pricked finger.

Destruction and reparation of blood in first attacks and in relapses.—There appears to be no very definite or manifest law governing the degree, progress, and quality of the anæmia of malarial disease. On the whole, and as rough general rules, it may be laid down that in any given case the anæmia is in pro-

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portion to the severity of the febrile attacks; that, although the loss of corpuscles following first attacks is usually very marked, this loss is rapidly made good; that, although in relapses the loss of corpuscles is less than in first attacks, the tendency to reparation is also less.

Morbid anatomy: *Macroscopic.*—If the body of a patient who has died in the course of an acute attack of malarial disease be dissected, certain appearances are generally found. In the first place, and invariably, the *spleen* is enlarged—often very much enlarged; its surface is dark—black sometimes; what is called pigmented. On section, the gland tissue is also found to be dark. Generally the parenchyma of the organ is so much softened as to be almost diffluent, so that the tarry pulp can sometimes be washed away by quite a gentle stream of water. The *liver*, too, is softened, congested, enlarged, and pigmented. The vessels of the *pia mater* and *brain cortex* are full, and the grey matter may present a peculiar leaden hue. The *marrow* of the spongy bones, such as the sternum and the bodies of the vertebræ, is also dark and congested; and a similar state of pigmentation and perhaps congestion may be discovered in the *lungs, alimentary canal, and kidneys.*

Microscopic: Malarial pigmentation.—The pigmentation referred to is pathognomonic of malaria. On submitting malarial blood from any part of the body to microscopical examination, it will be found to contain grains of hæmozoin. Particularly is this the case with blood from the organs just mentioned; their microscopical sections will show (Plate II., Figs. 2, 3, 4), more or less thickly distributed in the blood, and within the cells of the endothelium of the arterioles and capillaries, minute grains, or actual blocks, of the same intensely black substance. For the most part the hæmozoin grains are enclosed in leucocyte-like bodies which are either clinging to the walls or lying loose in the lumen of the vessels. Here and there the pigmented bodies may be so aggregated together that they form veritable thrombi and occlude the vessels. It is possible that many of

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these bodies are not pigmented leucocytes, but are really dead and breaking-down parasites; for if the preparations were made within two or three hours of death—that is to say, when the tissues were quite fresh—it may be possible to see that the capillaries of some of the organs are full not only of hæmozoin but also of parasites, a very large proportion of the blood corpuscles containing them. Particularly is this the case with the spleen and bone marrow; often, too, with the brain, liver, epiploön, and intestinal mucosa. The spleen and bone marrow are further distinguished from the other organs mentioned by the position in which the hæmozoin occurs in them. In all organs the pigment is found in the blood-vessels, but only in these two organs is it found in the cells of the parenchyma as well, and outside and away from the blood-vessels. This extravascular pigment is either free, or it lies in the large cells characteristic of these organs, or in the small cells of the parenchyma.

Nature and source of malarial pigment.—In colour, in structure, and in chemical reaction this pigment corresponds exactly with the pigment already described as forming so prominent a feature in the malaria parasites themselves. Like this, it is insoluble even in strong acids; it is altered by potash, and is entirely and rapidly dissolved by ammonium sulphide. In recent infections it occurs as minute dust-like grains; in infections of some standing as coarser particles, or as agglomerations of these into irregular, mammillated lumps. So far as the circulation is concerned, such a pigment is found in no other disease whatever. As an extravascular pathological product a similar pigment is found in certain melanotic tumours; but only in the cells of the tumour, never in the blood-vessels. Pigments of several kinds are found in old blood clots; but such pigments are manifestly different from that of malaria, and yield very different chemical reactions. Intravascular black pigment, therefore, is absolutely pathognomonic of malaria.* Because of

* The pigment-like dot occurring in a large proportion of the lymphocytes in normal blood (see p. 38) must not be confounded with malarial pigment.

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its physical characters, and of the circumstances in which it occurs, hæmozoin may with confidence be regarded as the specific product of the malaria parasite itself.

Source of the pigment in the pigmented leucocyte.—If further evidence be required of the identity of the intraparasitic pigment and that found in the tissues, it will be supplied by a study of the fate of the pigment grains and clumps set free in the blood on the breaking up of the segmented parasite.

If malarial blood, drawn during the rigor and early stages of acute attacks, and even at other times, be examined, large mononuclear leucocytes carrying grains or even blocks of black pigment may be encountered. If the observer be fortunate and persevering he will sometimes actually see whence this pigment is derived; he may even detect the leucocytes in the act of taking it up. He may see the pigment set free in the liquor sanguinis by the falling to pieces of a segmenting parasite; and he may then see a phagocyte creep across the field of the microscope and slowly engulf the little block. This undoubtedly is a principal source of the pigment in the leucocytes. Other, though possibly less important, sources are the effete gametes and, especially in the large cells of the spleen, necrosed parasite-containing red blood corpuscles.

Phagocytosis in the spleen.—The evidence of phagocytosis in the spleen in malaria is very remarkable. Not only are large and small masses of hæmozoin included in the macrophages, in the smaller cells, and in the endothelium, but entire blood corpuscles, sometimes as many as eight or nine, mostly containing parasites, besides free parasites, free hæmozoin, and fragmented hæmoglobin, are frequently to be seen in one and the same phagocyte. Sometimes one hæmozoin-laden phagocyte may be seen included in another phagocyte, and these perhaps in a third.

Blood of the splenic vein and liver.—Of all the vessels of the body the splenic vein is that in which malarial pigment is most abundant. Whereas in other vessels it is found to be included in ordinary leucocytes

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in this vessel it is included, not only in the leucocytes, but also in certain large white cells identical with those occurring in the spleen, and, doubtless, of splenic origin also. Similar cells may be found in the capillaries of the liver, rarely, however, in the blood beyond this organ; that is to say, they are filtered out by the liver from the blood carried to it by the splenic vein. An additional reason for the abundance of hæmozoin in the splenic vein is, that not only is the spleen the physiological destination of many of the hæmozoin-laden leucocytes and effete parasite-infested corpuscles, but it is likewise a favourite nursery for the parasite. In fact, the parasite is present in this organ in greater profusion than elsewhere. Hence it is that the splenic vein, coming direct from a rich breeding- and dumping-ground, contains a large number of hæmozoin-laden leucocytes.

Extravascular pigment.—In the early stages of malarial disease, except in the case of the spleen and bone marrow, the pigment is entirely confined to the lumen of the vessels and to their endothelium. But if we examine tissues from a case which has died at a late period of the disease, the pigment may then be found, not only in the endothelium, but also in the walls of the vessels, and even in the perivascular lymph spaces, whence, it may be inferred, it is subsequently carried to the lymphatic glands to be finally dealt with and broken up. As encouraging this view about the ultimate fate of the malaria pigment, Kelsch has pointed out the significant fact that the lymphatic glands in the hilum of the liver are always markedly pigmented in old-standing malarials; a fact evidently referable to the disposal of the large quantities of hæmozoin which, as we have seen, the liver filters out, more especially from the splenic portion of the portal stream.

These facts explain malarial pigmentation and oligocythæmia.—The facts just mentioned explain the origin and nature of malarial pigmentation, and also, in part at least, the oligocythæmia of the malarial state, which, as pointed out, is only partially accounted for by the destruction of corpuscles by the

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parasite in the general circulation as represented by finger blood. They show that what is seen in finger blood does not represent anything like the aggregate mortality going on among the corpuscles from direct destruction. The principal part of the malarial drama is played out in the spleen, liver, bone marrow, brain, etc., and not in the general circulation. What is seen in finger blood is but an overflow, as it were, of the greater drama going forward in the viscera.

The yellow pigment.—Besides the pathognomonic black pigment (hæmozoin), there is usually found in the organs a greater or less amount of a yellow or brown pigment (hæmosiderin), the "pigment ochre" of Kelsch and Kiener. This pigment is found not only in the capillaries, but also, and in greatest abundance, in the parenchyma cells of the liver, spleen, pancreas, kidneys, as well as in the bone marrow and in the connective tissues. It is not characteristic of malaria, but occurs in all morbid processes in which there is extensive breaking up of erythrocytes, as in paroxysmal hæmoglobinuria, in pernicious anæmia, in extensive burns, in poisoning by pyrogallic acid, potassium chlorate, arseniate of hydrogen, and many other toxic agents. It has peculiar chemical properties, being equally insoluble in acids, in alkalies, and in alcohol. At first, when freshly deposited, it gives no evidence, under the usual micro-chemical tests, of containing iron; after it has been in the tissues for some time it appears to be altered in character in this respect, and it then gives a ferrous reaction with ammonium sulphide, and with the double cyanide of iron and potassium.

Polycholia and hæmoglobinæmia.—Under ordinary conditions of physiological waste the products of the effete blood corpuscles are converted into bile pigment, and so got rid of. Up to a certain degree of pathological hæmoglobinæmia the liver can deal in a similar way with free hæmoglobin; so it comes about that, when this substance is free in the blood in unusual abundance, the secretion and flow of bile become correspondingly increased. If this flow

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of bile be excessive it gives rise to what are called "bilious symptoms"—bilious vomiting, bilious diarrhœa; symptoms which are so common in malarial disease, particularly in that variety known as "bilious remittent." Thus polycholia is a constant and often urgent feature in most malarial fevers, and is good evidence that in malarial infections there is a surcharge of the blood with free hæmoglobin. It is not improbable, although this point is disputed, that the yellowness of the skin and scleræ observed in these fevers is due to tinting by free hæmoglobin, to a hæmoglobinæmia in fact, and not, as is popularly believed, to biliousness or cholæmia from bile absorption.

The yellow pigment is deposited in excessive hæmoglobinæmia.—As in those other conditions referred to as being attended by rapid hæmolysis, in severe malarial fevers in which there is great and sudden liberation of hæmoglobin which the liver cannot at once deal with, pending its transformation into bile pigment the liberated hæmoglobin is taken up by the protoplasm of the cells of the different tissues and organs of the body, and precipitated in them in a slightly altered form; it is stored up in fact, waiting to be worked off as bile pigment by the, for the time being, overtaxed liver. The yellow pigment is, in all probability, this precipitated hæmoglobin.

Great excess of hæmoglobinæmia results in hæmoglobinuria.—Should the liberation of hæmoglobin go beyond this, be too great and too suddenly effected for the excretory powers of the liver and the storage capacity of the tissues, then the hæmoglobin, little altered in composition, seeks a more speedy way of escape by the kidneys, and hæmoglobinuria is produced. This is what is found in ordinary paroxysmal hæmoglobinuria, and in toxic hæmoglobinuria; and in this way we may account for the peculiar features of the disease to be described later on—hæmoglobinuric fever.

Size and shape of the blood corpuscles.—On the whole, in malaria, as in most anæmic conditions, the corpuscles are larger than normal—particularly those

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attacked by the parasite, especially the tertian parasite. Occasionally we come across genuine megalocytes, and, not unfrequently, certain very minute, darkly-coloured spherical corpuscles, which may be nucleated and of embryonic type. Erythrocytes with basophilic stippling are not uncommon. Some pathologists regard these basophilic granules as evidence of degeneration of the erythrocytes; P. Schmidt, on the other hand, considers them as evidences of regeneration, because in this, as in other forms of anæmia, they are most numerous during recovery. There may be marked irregularity of outline in many of the corpuscles and an indisposition to form rouleaux.

The leucocytes in malaria.—The leucocytes, espe cially the large mononuclear, play a very important part in malaria. In mild attacks their numbers, as observed in peripheral blood, decrease somewhat, both relatively to the red corpuscles and absolutely. In benign tertians and quartans their maximum is attained, according to Billings, two or three hours after the onset of chill. From this time there is a progressive diminution until the minimum is reached at the end of the paroxysm and when temperature has become subnormal. After this the number rises somewhat, and during the interval occupies a position midway between the maximum and minimum. The large mononuclear elements are increased, both absolutely and relatively. Sometimes the mononuclear are as numerous as the polynuclear leucocytes, especially during apyrexia. A mononuclear leucocytosis, of 15 per cent. and upwards, Christophers and Stephens regard as strong evidence of a malarial infection. With regard to the leucocytes in that type of fever which is caused by the crescent-forming small parasites, it is impossible, Billings says, to arrive at so definite a conclusion as in the cases of benign tertian. In the former type of case there appears to be a slight diminution in the number of leucocytes towards the end of the attacks, a diminution which is made good during the interval. Curiously enough, in certain severe per-

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nicious attacks there is a decided increase of the leucocytes in the peripheral blood—sometimes an enormous increase, a positive leucocytosis, the normal 8,000 per c.mm. rising to 10,000, or even to 30,000, the proportion to red corpuscles rising from 1 to 300 to 1 to 70.

The cause of fever and of periodicity in malaria.—The cause of fever in malaria is probably some toxin liberated when the segmented parasites break up in the blood. Celli's experiments failed to demonstrate the presence of such a toxin. Although he employed injections of large quantities of malarial blood serum, it is quite possible that this amount, large though it may have been, was insufficient.

The cause of the periodicity is doubtless of a two-fold character, the first and most important being the more or less fixed life-span of the parasites, and the second some physiological property in the human body which tends to destroy the parasites. Like so many physiological phenomena, this malaria-destroying principle or force has a tendency to quotidian increase and decrease. Although sometimes almost powerless to cope with the parasites, it usually brings about, especially after repeated infections, a more or less complete immunity.

It might be urged that though such an explanation may be applicable to quotidian periodicity, it could not apply to tertian or quartan periodicity. This cannot be admitted. If there be a regular quotidian occurrence of susceptibility to the malaria germ, this susceptibility must be existent on the second and third day as well as on the first; therefore a tertian parasite, on maturing, will encounter it on the second day, and a quartan on the third, just as certainly as if they were daily maturing quotidian parasites.

This hypothesis may be a wrong one. But although it may be wrong, it will not be without its use if it impress the importance of placing malarial patients under tonic influences as an aid to specific treatment; and, on the other hand, of protecting the subject of malarial recurrences from debilitating

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influences. For just as tonic influences may suffice to cure a fever, so, in many malarials, depressing influences—as a wetting, a surfeit, over-fatigue, anxiety, grief, in fact physiological strain of any description—are sufficient to provoke relapse of fever: presumably by debilitating or, for the time, abolishing the protecting physiological element which holds in check the latent but not extinct infection.

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CHAPTER V

MALARIA: MALARIAL CACHEXIA, ETC

MALARIAL cachexia is the term applied to a group of conditions, more or less chronic, believed to be the result of an antecedent attack of severe malarial fever, or of a succession of such attacks, or of prolonged exposure to malarial influences.

Undoubtedly many of the morbid conditions which were formerly attributed to the malaria parasites are the outcome of infections by *Trypanosoma gambiense* or by the Leishman body.

Symptoms.—The leading symptoms are those of a special kind of anæmia, characterised objectively by a peculiar earthy sallowness of skin, somewhat yellow sclerotics, enlargement of the spleen and—in the early stages at all events—of the liver. Usually the subject of this cachexia is liable to frequent attacks of an irregular type of fever, particularly after exposure or fatigue, or, in fact, after any unusual physiological strain.

Malarial cachexia without fever.—It should be mentioned that fever is not a necessary antecedent or accompaniment of malarial cachexia. In highly malarious countries it is not unusual to see typical examples in which fever had never been a feature, or, at all events, had been of so mild a character as not to have seriously attracted attention, or had occurred in childhood and been forgotten.

Enlarged spleen.—In such countries a large proportion of the population have enormously enlarged spleens. The traveller cannot fail to be struck by the number of people he sees with big bellies and spindle shanks; by their languid and depressed air; their sallow, dry, rough, unhealthy-looking skins. In many malarial cachectics the skin pigmentation is remarkably dark; patches of almost black pigmenta-

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tion are also sometimes discoverable on the tongue and palate.* It is said that in some intensely malarial places children are occasionally born with enlarged spleens, as if the malarial poison had already affected them *in utero*. I cannot personally vouch for this, but I have often seen very young children with bellies enormously protuberant from distended spleen. According to Scheube, De Freytag and Van der Elst observed in 1873 and 1878 in Atchin that all the children born were affected at the time of birth with malarial cachexia, and that most of them died in a few months. Bein and Kohlstock found malaria parasites in the blood of the four months' old child of a malarial mother, born some time after the arrival of the latter in a non-malarial district. Bignami failed to find malarial parasites, malarial pigmentation, or other sign of paludism in the fœtus of a woman who died of a pernicious malarial attack, an observation which has been repeated and confirmed by other pathologists.

Delayed development. — In some instances of malarial cachexia of early development the general growth of the body is stunted and puberty retarded. I have seen a malarial cachectic who, although twenty-five or twenty-six years of age, had the stature and sexual development of a child of eleven or twelve. Abortion and sterility are common effects of malarial cachexia, which, in this and in other and more direct ways, becomes a potent agent in repressing population.

Acquired tolerance of the malarial toxin. — In many instances, although the state of cachexia may have attained an excessive degree, ague, or, in fact, fever of any kind, has never been a prominent symptom. It would seem that the body can become accustomed to the fever-producing toxin of the malarial parasite, much in the same way that it may become accustomed to opium and many other organic poisons. I have watched for three weeks the rhythmical development of a tertian parasite in a sailor who, although previously the subject

* Observations in India tend to show that this condition melanoglossia, is racial and not pathological.

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of frequent attacks of ague, was quite free from fever during the period I had him under close observation. Just as in those habituated to the use of opium, a full dose of the drug, which in the unhabituated would produce profound or even fatal narcosis, acts merely as a gentle stimulant; so in those constantly exposed to, and actually infected with, malaria from infancy, the poison sometimes fails to act as a febrogene. And, to continue the comparison, just as the habitual use of opium produces a species of chronic poisoning or cachexia without narcosis, so the habitual presence of the malaria toxin may produce its peculiar cachexia without giving rise to fever. As a rule, however, particularly in the case of Europeans forced to reside in highly malarious countries, attacks of fever are of frequent occurrence in malarial cachectics.

Malarial neuroses and skin affections.—Superadded to the febrile attacks, and to the associated anæmia, we may meet in cachectics with a variety of functional troubles. One characteristic of most of these functional troubles is the periodicity they generally observe. Thus we may have quotidian, tertian, or quartan neuralgias, gastralgias, vomiting, diarrhœa, headaches, attacks of palpitation, of sneezing, and so forth. Besides these, skin eruptions—such as herpes, erythema nodosum, patches of lichen planus, eczema, urticaria, possibly synovitis—exhibiting a periodic liability to exacerbations and an amenability to quinine, have been noted in malarial conditions.

Peripheral neuritis.—I frequently see cases of well-marked peripheral neuritis, especially in patients from the West Coast of Africa, whose symptoms have been attributed to malaria. The degree of paresis varies from total inability to stand to weakness merely. There can be no question about the antecedent malaria, but whether the neuritis in every instance be the direct result of this infection it is hard to say. Lately I saw a well-marked multiple peripheral neuritis, in which there was slight fever with abundant sub-tertian parasites, promptly subside on the administration of quinine. In this case the

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neuritis began with violent cramps in the legs. Loss of memory, partial or complete, appears to be a common accompaniment of this condition.

Herpetic eruptions are very common in malarial attacks. According to Powell, in Assam the appearance of a patch of herpes somewhere about the body, usually the lips, is regarded as an infallible sign that the attack of fever is over for the time being.

Hæmorrhages. — In high degrees of cachexia hæmorrhages of various kinds are apt to occur; in such conditions epistaxis, hæmoptysis, hæmatemesis, melæna, retinal hæmorrhages, purpura, occasionally hæmaturia or hæmoglobinuria are not infrequent. In such patients trifling operations —tooth extraction, for example — may prove a dangerous matter. I have seen in malarial cachectics hæmorrhages from the latter cause which were very difficult to control. Care must therefore be exercised in advising and in performing even the slightest operations on patients of this class.

Intestinal and pulmonary affections.—In addition to the troubles mentioned, we find that the subjects of malarial cachexia are apt to be dyspeptic; to suffer from irregularities in the action of the bowels; to suffer from morning diarrhœa, at first of dark bilious, and later, perhaps, of pale, copious, and frothy stools. They are also very liable to a low and highly fatal form of pneumonia.

Cachexia associated with functional and with organic lesion.—There may be said to be two degrees or kinds of malarial cachexia. In one there is merely anæmia with congestion of the portal system; this may be quickly recovered from on the patient being removed from endemic malarial influences and subjected to specific and proper treatment. In the other there is, in addition to anæmia, organic disease of the abdominal viscera—of the liver, spleen, and kidneys —the outcome of long-standing congestion of these organs. These tissue-changes not only keep up the anæmia, in spite of removal from malarial influences, but, in the long run, inevitably progress to a fatal issue.

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Pathology and pathological anatomy.—The pathology of malarial cachexia is virtually, in the first instance, that of acute malarial disease. There is blood destruction by the direct action of the malaria parasite and of its toxins, eventuating in oligocythæmia and in the deposit of hæmozoin and of hæmosiderin (yellow pigment) in the tissues. The activity and persistence of the process lead to congestion which ultimately determines organic changes in liver, spleen, kidneys, and probably in the bone marrow.

Splenic enlargement.—The spleen may become so enlarged under repeated attacks of the congestion attending a succession of fever fits, or in consequence of a less active and perhaps feverless hæmolysis, that it may come to weigh many pounds, and so to increase in bulk as to occupy nearly the entire abdomen. The capsule of the gland, particularly on its convex surface, is thickened, and, perhaps, the seat of fibrous patches, or even of adhesions to neighbouring organs. Many of the trabeculæ forming the framework of the gland become greatly hypertrophied. On section, the tissues of such a spleen are found to be moderately firm, and usually of a reddish-brown colour; but when death happens soon after or during a febrile attack, the section of the gland shows a dark surface from deposit of hæmozoin, the pulp at the same time being softened. Perhaps from over-distension some of the vessels in the interior of the gland give way, and then there is a breaking down of the spleen pulp in patches, the remains of splenic tissue floating about in the extravasated blood. Microscopic inspection of these hypertrophied spleens, especially during fever, shows the black and ochre pigments in the situations already indicated.

"*Splenic index.*"—There are practical points in connection with malarial spleen which deserve mention. The relative absence, or prevalence, of these enlarged spleens or "ague cakes" in the native population is an excellent rough indication of the salubrity or the reverse, as regards malaria, of any particular district. Wherever they are common the district is

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malarious and therefore unhealthy, perhaps to Europeans deadly, and should be looked upon as extremely unfavourable for camping or residential purposes.

Liability to rupture of splenic tumours.—Another practical point is that these enlarged spleens are easily ruptured by a blow on the belly. In hot and malarious countries many a coolie goes about doing his work although he has an enormous spleen. This is a fact to be remembered in administering even mild corporal punishment to natives of malarious countries. Europeans have more than once been tried for manslaughter in consequence of neglecting it. Owing to this liability to rupture, the subjects of splenic enlargement must not be allowed to play at violent games as football or even cricket, or at any game in which the diseased organ is exposed to a blow. Apart from direct violence, an enlarged spleen may rupture spontaneously, owing to sudden accession in size in the course of a fever fit.

Splenic ruptures are, of course, generally fatal. It sometimes happens that the presence of adhesions limits and restrains the hæmorrhage. Localised hæmorrhages of this description may, in time, lead to splenic abscess.

Hepatic enlargement.—Like the spleen, the liver in malarial cachectics becomes enlarged during accessions of fever. Under the influence of a succession of acute attacks, hepatic congestion may gradually acquire a more or less permanent character. After death from such fevers the capsule of the liver is found to be tense; on section, the highly vascular tissue of the organ is seen to be reddish-brown or almost black, according to the degree and kind of pigmentation. If this stage of congestion be long maintained, it tends to bring about various kinds and degrees of chronic hepatitis with hypertrophy of the intralobular connective tissue, and in time leads to hypertrophic or to different forms of atrophic cirrhosis. Thus irremediable organic disease of the liver, portal obstruction, and ascites may ensue.

Siderosis.—It is in livers of this description that

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a form of what is called *siderosis* is produced—a condition resulting from chemical changes undergone by the yellow pigment with which the various cells of the organ are charged. It has already been stated that, when first deposited, this pigment gives no ferrous reaction with ammonium sulphide, or with the double cyanide of iron and potassium; and that, as the deposit becomes older, chemical changes ensue, resulting in the elaboration of a form of iron which will then yield the characteristic black colour with the former, and blue colour with the latter reagent. Treated with ammonium sulphide, sections of liver, and also of spleen, kidney, and other hæmosiderin-charged tissues from chronic malarials, may turn almost black to the naked eye, or, at all events, exhibit under the microscope abundance of blackened pigment. In such sections it is seen that the hæmosiderin is no longer in minute grains, as when first deposited, but in blocks and globules as large as, or even larger than, blood corpuscles. This pigment is, of course, something quite apart from the parasite-derived hæmozoin deposited in the same organs.

Practical considerations.—Certain clinical facts about malarial hepatic congestion and malarial hepatitis are of importance. (1) Such conditions do not tend to terminate in suppuration; (2) they are almost invariably associated with splenic enlargement. These are important facts to recollect when it becomes a question of the diagnosis of malarial hepatitis from abscess of the liver. Another important fact to remember is that recent malarial enlargement of the liver is usually curable, depending as a rule on simple congestion; whereas old-standing malarial hepatic enlargement is usually incurable, depending, as it usually does, on hypertrophy of the connective tissue and a cirrhotic condition of the organ.

Malaria a cause of nephritis.—Changes similar to those found in the liver in the course of, and in consequence of, malarial disease occur in the kidney; in time they result in confirmed Bright's disease. Hence, probably, the frequency of Bright's disease in some highly malarious climates. In the *British*

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Guiana Medical Annual, Daniels mentions that in 926 *post-mortem* examinations in the hospital at Georgetown, Demerara, a highly malarial district, he found evidence of disease of the kidneys in no fewer than 228.

Cardiac degeneration.—As a consequence of defective nutrition from prolonged anæmia and recurring fever, the muscular tissue of the heart in chronic malarials may degenerate, the ventricles dilate, and, in time, the lower extremities become œdematous. For the same reason the subjects of valvular affections of the heart, whether compensated or otherwise, are unsuitable for residence in malarial countries.

Other sequelæ.—Dysenteric conditions, forms of diarrhœa, low forms of pneumonia readily set up by chill and prone to terminate in abscess of the lung or to become associated with empyema, extensive sloughing phagedæna, and other forms of gangrene such as noma, or pernicious fever may supervene at any time and rapidly carry off the subject of advanced malarial cachexia.

Tubercular and syphilitic disease not unfrequently concur with malaria; in fact, the latter may powerfully predispose to local manifestations of either of the two former, and *vice versâ*, a complication as to which the practitioner must be on his guard.

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CHAPTER VI

MALARIA: ÆTIOLOGY

In considering the **ætiology** of malaria two things must be carefully distinguished: (1) the circumstances leading to the invasion of the human body by the malaria parasite; (2) the circumstances determining the clinical manifestation of such invasion.

CIRCUMSTANCES FAVOURING INFECTION.

In the mosquito-malaria theory, now thoroughly established, we have the key to this problem. Whatever favours the presence and increase of the malaria-bearing species of mosquito tends to the increase of malaria, and *vice versâ*; whatever favours the access of these insects, and the parasites which have passed into them, to the human body favours the acquisition of malaria.

It must not be forgotten that the malaria parasite, after giving rise to fever within a few days of its original invasion of the human body, tends to pass into a latent condition from which it wakes up into clinical activity again only after longer or shorter intervals; further, that in rare instances the clinical evidence of a successful malarial invasion may be delayed for months or, perhaps, for years. Consequently, the particular circumstances in which any given malarial attack declares itself are not necessarily those which led to the acquisition of the infection originally. Therefore, in regard to the ætiology of malaria, fevers of first invasion have a significance very different from that pertaining to relapses or recurrences.

Geographical range.—The geographical range of malaria is very great; it extends in the Northern hemisphere from the Arctic Circle to the Equator, and in the Southern probably as widely. Malaria is not uniformly distributed throughout this vast area. It

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occurs in limited endemic foci which tend, speaking generally, to be more numerous and larger as the Equator is approached.

Influence of latitude and season.—In colder latitudes the association of malaria with swamps is marked; in warmer latitudes this association is much less apparent. In colder latitudes the type of disease is milder; in warmer latitudes it is apt to be more severe. In certain warm countries, as the Argentine and many of the islands of the South Pacific, malaria is entirely absent, or mild and rare. In colder latitudes it is active only during the summer or early autumn; in warmer latitudes it is perennial, certain seasons—usually, though not invariably, the warmer, or after the rains—being the more malarial.

Influence of local conditions.—The strip of flat, waterlogged country lying along the foot of mountain ranges, the deltas of large rivers, the pool-dotted beds of dried-up streams, areas of country which have fallen out of cultivation, recently deforested lands, are, in many instances, notoriously malarial. Well-drained uplands and carefully cultivated districts, as a rule, are healthy. There are, nevertheless, instances of elevated, arid, and sandy plains which, under certain hydraulic conditions, are intensely malarial. Towns are much less malarial than villages or the open country.

Ship malaria.—Although several instances are on record of outbreaks of what was reputed to be malaria on shipboard on the open sea, many epidemiologists refuse to accept the diagnosis as to the nature of these outbreaks, and maintain that malaria is never contracted away from the land. Mosquitoes haunt ships for some time after the latter leave port. If they are infected with the malaria parasite when they first enter the ship, or if they ingest the parasite after coming on board, they may very well communicate malaria.

Endemic and epidemic fluctuations.—From time to time malaria extends beyond its endemic foci, spreading in epidemic form over large tracts of

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what is usually healthy country. There are a few well-authenticated instances of countries (Mauritius, Réunion) which, although previously exempt, subsequently became endemically malarial; and there are many instances of countries previously malarial which afterwards, especially under the influence of cultivation and drainage, became salubrious.

These circumstances evidently have reference to the distribution of species of malarial mosquitoes. Mosquitoes, like other insects, occasionally, under specially favourable conditions, increase enormously in numbers and spread out in every direction. New species, which may belong to the malaria-bearing kinds, may be introduced into places where they formerly did not exist, just as *Culex fatigans* has been introduced into Australia. I believe a mosquito capable of subserving the malaria parasite was introduced in this way in the early 'sixties into Mauritius, an island whose fauna and flora had been hitherto very peculiar and special. In this way we can account for the outbreak of the great epidemic of malaria that swept over that formerly healthy island and also for its present endemic insalubrity. A similar misfortune may very well happen to the South Pacific islands in the near future.

The exemption of certain islands from malaria, even though in the midst of an archipelago of malaria-haunted islands, is a very remarkable circumstance. Barbados is an instance in point. Low has confirmed the popular belief that malaria is unknown there as an indigenous disease, and points to the absence of Anophelinæ as the explanation. But how explain the absence of Anophelinæ, seeing that culex abounds and all the conditions favouring mosquito life are present? The disappearance of malaria from Britain is another remarkable, and perhaps not fully explained, fact. Anophelinæ still abound in many places, yet the endemic malaria has vanished. It may be that the general use of quinine and the improved domestic hygiene have to be credited with this. Still more remarkable is the circumstance that there are villages and districts in

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India, as pointed out by Christophers and Stephens, and similar districts in Italy, as pointed out by Celli, in which, though surrounded by highly malarious country and though Anophelinæ abound, yet there is no malaria. The explanation of this anomaly is not apparent. Perhaps in these places there is some local substance on which the mosquitoes feed that is fatal to the parasite. Sambon ingeniously suggests that there may be special local conditions that favour *hyperparasitism*, that is, the attack and destruction of the malaria parasite by some other kind of parasite. Similar occurrences are common enough in nature. In support of this view he cites Ross's observation of what he designated "*black spores*" (Fig. 25), bodies which are now known to be protozoal organisms belonging to the genus *Nosema*. These "black spores" prey on the malaria oöcyst in the wall of the mosquito's stomach and destroy it, just as they prey on the larvæ of *Filaria immitis* encysted within the malpighian tubes of the mosquitoes which subserve their development. Whatever the explanation of the salubrity of these mosquito-haunted plains be, it is well worth searching for; it may be that it would carry a hint of value in attempting the prevention of malaria.

Fig. 25. — Ruptured oöcyst containing Ross's black spores. (*After Grassi.*)

Atmospheric temperature.—One of the most important conditions necessary to the sporogonic phase of the malaria germ is a sustained average temperature of at least 60° F. The malaria parasite will not develop in the mosquito at low temperatures.

Altitude.—Altitude *per se* has, apparently, no influence on malaria. It is the decrease in temperature, usually implied by an increase in altitude, that is the real determining circumstance in bringing about a diminution in the prevalence of malaria in uplands. In the tropics an elevation of six or seven thousand feet may not secure immunity from malaria unless there be, at the same time, a corresponding and

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sufficient lowering of temperature. In Italy there are many malarious spots high up among the hills; the same is the case in India and elsewhere in those elevated valleys which are also narrow, imperfectly ventilated, and imperfectly drained.

Moisture.—Another important condition for the production of malaria is the presence of water. In the Sahara there is no malaria unless in the oases; in many of these it is rife—in Biskra, for example. A large expanse of water is not favourable to malaria. The mosquito thrives best in sluggish streams with grassy banks and many backwaters; still better, in small pools or other collections of water, as in broken bottles, empty tins, etc., where there are no fish to prey on their larvæ, and where the surface is not agitated by winds. One such puddle near a house may suffice to render that house unhealthy.

Decomposing vegetable matter.—It is customary to add yet another condition as being necessary to the existence of malaria—namely, the presence in the soil of a notable amount of decomposing organic matter, particularly vegetable matter. But that this is not an indispensable condition is proved by the fact that there are many almost barren spots in which malaria abounds.

Other conditions necessary. — The concurrence of these conditions, high temperature and moisture, even though associated with abundant vegetation, is not sufficient to generate or support malaria; for there are many places in the world—the Argentine and the islands of the South Pacific, for example—in which high temperature, moisture, and decaying vegetable matter are present, but in which malaria is almost unknown. Manifestly there are other and more complicated conditions which are equally indispensable, and which must concur with heat and moisture in order to secure the presence of malaria-bearing mosquitoes. What these conditions are it is as yet impossible to say.

Influence of subsoil moisture.—The state of the subsoil as regards moisture appears to have considerable influence on its malaria-producing properties.

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Short of general overflow, the higher the subsoil water the greater the chance of a given locality supplying breeding places for mosquitoes and therefore of proving malarious. Hence arises marked liability to epidemics of malaria on the subsidence of extensive floods; and hence the danger attending the raising of the level of the subsoil water by irrigation works, canals, embankments, and other engineering works.

Influence of rainfall.—As regards the relation of the prevalence of malaria to rainfall there have been too many generalisations based on the limited experience of one or two districts. Thus, it is often said that the most malarious time of the year is at the end of the rains, when the soil is beginning to dry up. A wider view of the subject shows that, though applying to some places, this statement does not apply to all. There are localities where the fever curve is highest before the setting in of the rains. In some places, particularly in those that are low-lying, flat, and swampy, fevers of first invasion disappear almost entirely when the country becomes flooded. This apparent want of a universal and definite relationship of fever curve to rainfall indicates that the conditions determining the prevalence of malaria are highly complex, and that they are not by any means merely a matter of heat, moisture, and vegetation. In some places much rain will scour out the mosquito pools; in other places it will just fill them. The key to the explanation of the varying relation of malaria to rainfall is to be found in the influence of the latter on the local mosquito pools.

Influence of winds and atmospheric diffusion.—It has been said that the wind can carry the malaria germ great distances, roll it along the ground like thistledown, and even force it to ascend high mountains. It is very doubtful, however, if the malarial mosquito can be transported, in this way, very far from its native pool. The mosquito does not ascend more than a few feet from the ground, and in high winds, or even in draughts of air, such as that from a punkah, immediately seeks shelter. It is certain that

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some thousand or fifteen hundred yards of water between a ship and a malarious coast suffice to secure immunity to the crew. The experience of the notorious Walcheren expedition proves this. A similar distance on land from a malaria source is probably approximately as effective. The diffusion of malaria by winds is probably extremely restricted. Inside, a city may be quite healthy, whilst outside the walls the country may be pestilential. One village may be sickly, whilst a neighbouring village may be healthy. Surely, if winds transport the malarial germ for any distance from its source, there would not be so great a difference in the relative salubrity of urban and suburban localities, nor of neighbouring houses and villages. Neither does the malaria germ ascend to any great height above the ground. Acting on the empirical observation of this fact, the peasants in many unhealthy spots in Italy and Greece are said to secure a remarkable degree of immunity by passing the night, during the fever season, on platforms raised on poles a few yards above the ground. It seems safe, therefore, to conclude that the horizontal and vertical diffusion of the malaria germ—that is to say, of the mosquito—is very restricted.

Influence of trees, houses, and lodging.—The intervention of a belt of trees between a malarial swamp and a village is said to protect from malaria the houses on the leeward side of the trees. The trees may filter out the mosquitoes by affording them protection from winds. Open windows and doors, by giving ready access to mosquitoes, are sources of danger in malarial countries; for this and similar reasons sleeping on the ground, on the ground floor, or unprotected by a mosquito curtain, is dangerous.

Time of day in relation to infection.—Evidently in conformity with the habits of the mosquito, the time just before sunrise and just after sunset, and the night, have the reputation of being the most dangerous as regards liability to contract the infection. Although mosquitoes are most active during twilight and night, they bite readily enough during the daytime

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in shady and windless places, as in thick jungle or in a dark room. A very few species are diurnal in habit.

Disturbance of the soil.—It has often been observed that in malarious countries, so long as the soil remains undisturbed, agues and the severer forms of fever are comparatively rare; but so soon as building, road-making, and other operations implying soil disturbance commence, then severe malarial fevers appear. After a time, and when these operations in the progress of events have concluded, and the broken surface of the soil has, so to speak, skinned over again, the place becomes once more comparatively healthy. The medical history of Hong Kong may be cited in illustration of this fact. At the commencement of the occupation of this island by the British, for a short time it was healthy enough. Then, on its cession being completed, and when barracks and houses were being built and roads laid out, it became excessively unhealthy, the soldiers dying by the hundred of pernicious fevers. In time the sickness and mortality gradually decreased; and now, so far as malaria is concerned, the city of Victoria is healthy. But, even at the present day, wherever in the outskirts, in the course of the construction of houses, roads, forts, and similar works, soil is turned up, fever—often of a most pernicious type—is nearly sure to break out among those engaged in the works. I cite the case of Hong Kong; but there are dozens of other instances which might be quoted, and which are quite as apposite and convincing, as to the danger of carelessly disturbing the soil in malarious localities, particularly during the warm season. Soil disturbance usually implies the formation of holes. Holes imply puddles, and puddles imply mosquitoes. Workmen from many districts, some of them malarious, are assembled in crowded lodgings; one infected workman suffices to start the epidemic. In the present state of knowledge this seems to be adequate explanation of the recognised danger of earth-cutting in malarious districts.

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CIRCUMSTANCES FAVOURING THE CLINICAL MANIFESTATION OF MALARIAL INVASION.

As a rule, a successful infection declares itself within a week or ten days. As with other infections, certain individuals resist invasion by the malaria parasite for a longer or shorter period. A very few appear to be permanently immune. Everything tending to cause physiological depression favours susceptibility and acute manifestations.

Influence of meteorological conditions on relapse.—A malarial subject while in the mild climate of the tropics may keep in fair health; but when, as is so often the case with sailors and others returning to Europe, he is plunged into the stormy winter of the North, is exposed to cold, and has long watches and fatiguing work, very probably latent malaria will become active and ague follow. This is a common experience with malarials from the tropics. It is almost the rule with people coming from the West Coast of Africa. Stanley says that so long as he and his companions were ascending the Congo, the wind being with them and therefore not much felt, they did not have fever; but that on descending the stream, a strong breeze blowing in their faces and chilling them, they constantly had attacks. The physiological depression and disturbances caused by the cold wind paralysed the self-protecting power of the body, and permitted the hitherto latent parasite to get the upper hand. And so it is found, in the highly malarial districts of tropical Africa, that houses perched on elevated and windy situations are not so healthy as those on lower and, therefore, less exposed and more sheltered ground. This must not be interpreted as showing that wind causes or carries malaria. The wind merely acts as a cause of physiological strain, of chills; it acts just in the same way as fatigue, hunger, a wetting, disease, fear, excesses, or depressing emotions are found to do.

Sex, age, occupation.—Sex, *per se*, seems to have no particular influence as regards liability to, or severity of, malarial attacks. Neither has occupa-

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tion; although, of course, those engaged in tilling and working the soil are more exposed to mosquito bite, and therefore more subject to malaria, than the townsman or the sailor. Malarial attacks are more severe, more common, and much more dangerous in young children than in adults.

Malaria a communicable disease.—Malaria is certainly not directly communicable, in the same way that such diseases as small-pox or measles are. It can be communicated directly only by injection of malarial blood. But there can now no longer be any doubt that a malarial patient introduced into a community, provided suitable mosquitoes are present, is a source of danger. If mosquitoes of the proper species bite such a patient—say in the wards of a hospital, in a jail, a house, or a camp—and a week later bite someone else, that second individual may become infected, and ten days later may be seized with malarial fever.

Study of the mosquito indispensable.—Full knowledge of all that concerns the ætiology of the disease will only be attained when we have full knowledge of the various species of mosquito capable of subserving the germ, of certain vertebrates which may be capable of taking the place of man in the malarial cycle, of their geographical distribution, of their habits, and of their enemies. As yet this knowledge is but beginning. When we have said that the malaria parasite is subserved by several species of Anophelinæ and that these species are mainly of nocturnal habit, we have enumerated the principal items of existing knowledge on the subject. Whether certain species of Culex, Stegomyia and other Culicinæ may not be efficient hosts for the parasite, as some of them certainly are for *Plasmodium danilewskyi* and *Filaria bancrofti*, can as yet neither be affirmed nor denied. Studies in this field are being actively carried on, and important advances may be looked for.

ACCLIMATISATION AND IMMUNITY.

Personal acclimatisation.—Is there such a thing as acquired immunity as regards malaria? The

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answer to this is, "Yes and No." As regards the European, it would seem that those who have resided many years in a malarious district are less liable than recent arrivals to severe remittents, but more liable to mild agues. As already mentioned, the first attack of malarial fever is generally remittent and severe in character; subsequent attacks are generally frankly intermittent. Old febricitants are more liable to pernicious attacks of an adynamic type than the recently infected. Trifling causes, such as do not provoke fever in the fresh arrival, are often sufficient to bring on an ague fit in the old resident. The new arrival in the tropics does not think much of exposing himself to the sun, the rain, and the wind; but the old resident is very chary about going out without his sun-hat and white umbrella. The latter wears flannel, and changes his clothes after exercise; he is careful not to cool off too rapidly by sitting in a draught; he will not sit down in wet clothes. The newcomer may look on these precautions against chill as signs of effeminacy. They are not so, however; experience has taught the old resident that neglect of them means an attack of fever and a week off work. The newcomer takes a cold bath; the old resident takes a warm one. The newcomer sits up late, eats and drinks and smokes as in Europe; the old resident goes to bed betimes, and eats and drinks and smokes in moderation. By-and-by, sharp lessons teach the newcomer to respect the sun and the rain and the wind, to clothe with a view to avoiding chill, and to live temperately. This is an education all pass through in malarial countries. "Acclimatisation," to a great extent, though not entirely, means experience, education; not simply an unconscious adaptation of the physiology of the individual, but an intelligent adaptation of his habits.

Racial and individual differences of susceptibility. — Nevertheless, there can be no doubt that, for some occult reason, certain races and certain individuals are less susceptible to malarial influences than others. A very few individuals are absolutely immune and can live in

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intensely malarial places with impunity. It is a well-established fact that the negro in Africa, although he does get fever, does not get it so frequently nor so severely as the European; even although the latter, from his hygienic ways of living, is of the two much the less exposed to infection. The Chinese, the Malays, and some other dark-skinned races also appear to enjoy a comparative immunity—an immunity considerably less pronounced, however, than that enjoyed by the African and West Indian negro. There is some evidence to show that even the individual European, if he survive the process, may after many years, through frequent infection, attain immunity; this, however, does not appear to be transmitted. The inhabitants of the malarious districts of Italy, Corsica, Greece, Turkey, and other South European countries have inherited no marked immunity from malaria in virtue of the thousands of years during which their ancestors lived in malarious districts. But they have inherited experience, and many of them know how to keep clear of the infection they cannot overcome; this probably is, in great measure, the extent of their acclimatisation and apparent acquired immunity.

We are indebted to Koch for an important observation, with manifest practical bearings, on this subject; an observation which throws light on the apparent immunity of negroes, Melanesians, and other dark-skinned races living in highly malarious countries. He has shown, and his statements have been abundantly confirmed, that the natives of such districts acquire their immunity from repeated and persistent infection in childhood. In such places the blood of practically every child up to three or four years of age contains malaria parasites. The proportion of infected children gradually becomes smaller with each additional year, until adolescence is approached, when the blood becomes practically parasite-free, and immunity is established. Daniels had already shown, by a comparative study of the prevalence of malarial pigmentation in the cadavers of natives of British Guiana, that such was probably

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the case; Koch's more direct observations on the parasite in Melanesia, confirmed as they have been by English observers in India and Africa, have definitely settled the matter.

The mortality in native children from malaria is very great; but it would appear that a relative tolerance is soon acquired, for although the negro child may have a rich infection of parasites in its blood, possibly in consequence partly of increasing immunity, partly of some racial and inherited quality, it may exhibit a remarkable tolerance of the malaria toxins. It has often been remarked that these dark-skinned children, with enormous spleens and a rich stock of malaria parasites in the blood, run about fever-free, and apparently in rude health. It would seem that certain races of men react to the malaria parasite much in the same way as the Texan cattle react to *Babesia*, or as the large game animals of Africa react to *Trypanosoma brucei;* repeated infection in early youth, if it does not quickly prove fatal, creates immunity. Race may have something to do with the tolerance of the infection; but it is not everything, for the negro from a non-malarial country on becoming infected in a malarial country suffers almost as severely as the European.

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CHAPTER VII

MALARIA: DIAGNOSIS

THERE is a marked tendency to regard and diagnose all fevers occurring in tropical countries, or in individuals who have returned from tropical countries, as malarial. Such slovenliness in diagnosis must be strenuously avoided by the practitioner. It is apt to become a habit which, sooner or later, is bound to have disastrous consequences.

The three pathognomonic signs of malaria.—The diagnosis of malarial disease, if all the means at our disposal be employed, is usually not a difficult matter. Formerly, periodicity and the effect of quinine were the tests principally relied on. In certain circumstances they are fallible. Nowadays, in all doubtful and serious cases, it behoves the practitioner to have recourse to the least fallible test — the microscopic examination of the blood. When such an examination yields a positive result, when the parasite in any of its forms, or its characteristic product—hæmozoin—either free in the liquor sanguinis or enclosed in leucocytes, is found, the diagnosis of malaria is securely established. Negative results from a single microscopical examination are not so trustworthy as positive; but if the practitioner has experience, and if he has the opportunity to make his examinations at suitable times and in a case untreated by quinine, they, too, are conclusive, more especially if supplemented by a differential count of the leucocytes.

The quinine test is generally conclusive in intermittents and in the various larval forms of malaria, but the more severe types of remittents are often singularly resistant to the drug. Moreover, time may not be available in which to test such cases with quinine. They may be cases of a threatening nature

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in which a speedy diagnosis is of the first importance. In such cases the microscope is the only available trustworthy diagnostic agent.

Periodicity in diagnosis. — Periodicity at times is a trustworthy enough clinical test for malarial disease. *Tertian and quartan periodicity occur only in malarial disease;* when either is thoroughly established, its presence is almost conclusive as to the case being malarial. It is otherwise as regards the significance of quotidian periodicity. Quotidian periodicity we find in greater or less degree in nearly all fevers, particularly in fevers associated with suppuration. In hectic conditions quite unconnected with malaria one often sees a quotidian afternoon rigor, followed by hot, dry skin, and a temperature rising even to 103° or 104° Fahr., the febrile movement concluding with a profuse diaphoresis and complete morning apyrexia.

Periodicity of fever in liver abscess; diagnosis from malaria.—Particularly is this the case in suppuration connected with the liver—a condition peculiarly liable to occur in tropical practice. Simulation of malarial fever by hepatic abscess is very common; it is a pitfall into which the inexperienced tropical practitioner often tumbles. In consequence, we find that, at one time or another, most liver abscess cases are drenched with quinine, on the supposition that the associated fever is malarial. There are several points, even apart from an examination of the blood, which, if duly considered, will avert this blunder.

In hepatic abscess, although the liver is enlarged, the spleen is not necessarily so; splenic enlargement, though an occasional, is not a usual feature in liver abscess. In malarial fever if the liver be enlarged the spleen is still more so, and usually can be felt extending well beyond the costal margin. In hepatic abscess the fever occurs generally, though not invariably, in the late afternoon or evening; the patient may perspire profusely, independently of fever lysis, at any time of the day or night—very generally whenever he chances to fall asleep. In malarial

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fever the paroxysm may, and generally does, occur earlier in the day; there is no marked tendency to sweating unless at the defervescence of the fever. In hepatic abscess a history of dysentery is nearly always obtainable if carefully inquired for. If fever be distinctly tertian or quartan in type it is not hepatic. In all doubtful cases the blood must be examined once or oftener, the rigor stage or early hot stage being selected for the examination, and the examination being made before administration of quinine. Apart from the presence or absence of the parasite or of pigmented leucocytes, marked increase of polymorphonuclear leucocytes would be in favour of hepatic abscess; a relative excess of mononuclear leucocytes in favour, though not conclusive, of malaria. Occasionally cases are met with in which there is a history of malarial infection and, in addition to this, a history of dysentery, and the liver and spleen are both enlarged. In such cases diagnosis may be impossible without the microscope and the aspirator.

Diagnosis of bilious remittent from yellow fever.—In bilious remittent the icteric tinting of the skin is an earlier feature; albuminuria is not so common and generally not marked; temperature is maintained high for many days, not subsiding in three or four days as in yellow fever; the vomiting is profuse and bilious; the pulse does not become phenomenally slow as in yellow fever; in the initial stage the eyes are not congested and shining to the same degree; and, of course, the parasite is to be found in the blood.

Cerebro-spinal meningitis may simulate malarial fever; but the occurrence of rigidity of the muscles of the neck should put the physician on his guard, and lead him in such a case to search the blood and inquire for other diagnostic symptoms, as, for example, the respective leucocytic variations of the two infections.

Diagnosis from other types of paroxysmal fevers.—The following also are often mistaken for malarial fever:—Urethral fever; the fever attending

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the passage of gall-stones, or with inflammation of the gall bladder; that associated with pyelitis and surgical kidney; lymphangitis, particularly that form of lymphangitis associated with elephantiasis and other filarial diseases; Mediterranean fever; relapsing fever; trypanosomiasis; kala-azar, generally an irregular fever, though often quotidian, and almost invariably attended with enlarged liver and spleen and with anæmia; the fevers associated with tuberculous disease, with ulcerative endocarditis, with some types of pernicious anæmia, with splenic leucocythæmia, especially with visceral syphilis, with rapidly-growing sarcoma, with forms of hysteria, and with many obscure and ill-defined conditions. The use of the microscope must not be neglected in such cases if there be the slightest doubt as to their exact nature.

It must not be concluded that, although unquestionable evidence of the presence of one or more of the foregoing has been obtained, malaria is absent. Malaria often concurs with these diseases. Malaria is a common complication in trypanosomiasis, for example, and it is often hard to pronounce as to whether in such cases any given rise of temperature be due to the trypanosoma or to the malaria parasite.

Typhoid fever.—Without the microscope it is sometimes impossible to diagnose typhoid types of malarial fever from genuine enteric. In both there may be diarrhœa or constipation; in both there may be splenic enlargement; in both there may be typhoid tongue, delirium, and the entire range of typhoid symptoms. As a matter of fact, until recent years all typhoid in India was regarded and treated as malarial fever—malarial remittent—and, doubtless, often with disastrous results. In circumstances where the Widal test is available it is an invaluable supplement to microscopical examination of the blood.

Typho-malarial fever.—One important fact in connection with the diagnosis of typhoid in malaria must ever be kept in mind. In individuals who have previously been subjected to malarial influences and who, perhaps, have suffered at one time from well-marked malarial fever, the oncoming of typhoid is

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often preceded by three or four paroxysms exactly like those of ordinary ague. This may occur even when the patient has been for some time in a non-malarial country, as England. In such cases quinine is usually given early in the attack; its failure to check the disease should lead to careful prognosis and the avoidance of too active purgation. Similarly, well-marked malaria-like fluctuations of temperature and the appearance of the parasites in the blood in the course of a continued fever do not exclude typhoid. These cases are probably typho-malarial, and have to be treated as such—as typhoid with a malarial complication.

Necessity for microscopical examination of blood in pernicious attacks.—Without the microscope it is sometimes impossible to diagnose, in time to direct appropriate treatment, pernicious comatose malarial attacks from heat-stroke or, if algide in character, from ordinary apoplexy; malarial dysentery, which must be treated with quinine, from ordinary dysentery, which must be treated with ipecac., or with the sulphates; algide malarial attacks, from cholera; certain types of malarial fever, occurring, as it is very apt to do, in the puerperal state, from puerperal fever; malarial pneumonia, from croupous pneumonia; malarial aphasia, from the aphasia of organic brain disease; and so on.

It is manifest that the revelations of the microscope have enhanced our powers of diagnosis in malarial affections enormously, and, therefore, our powers of treatment. Every doubtful case must be tested by it. In many forms of malarial disease, if life is to be saved, action must be prompt, decisive, energetic, and based on accurate diagnosis. The diagnosis of ordinary agues may be postponed for a day or two without much danger, and be made correctly enough without the microscope; but every now and again a pernicious attack is sprung upon the practitioner, the nature of which he must be able to recognise at once, and recognise with confidence. When the parasite is seen in the blood, it is surely known that there is a malarial element in the

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case and that quinine is indicated. Confidence in directing treatment is a great matter. It cannot, therefore, be too strongly urged on the tropical practitioner to avail himself of every opportunity to gain experience in the use of the microscope in blood examinations, and to take care to have a suitable instrument in working order and available at a moment's notice. The practical difficulties in carrying out this recommendation are insignificant in comparison with the importance of the results. With practice, five minutes usually suffice to effect a positive microscopical diagnosis of malaria.

Every tropical practitioner should be provided with a travelling microscope, or, at least, carry about with him a few microscope slips for blood films. He must be on his guard, however, against concluding from the discovery of malaria parasites in his films that malaria is necessarily the only, or even the principal disease his patient is suffering from.

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CHAPTER VIII

MALARIA: TREATMENT

Quinine.—Many drugs have been employed in the treatment of malarial disease, and many drugs have some influence on it; all sink into insignificance in comparison with quinine. In serious cases, to use any drug to the exclusion of quinine is culpable trifling. Therefore, so soon as a diagnosis of malaria has been arrived at, unless there be some very manifest contra-indication, the first duty of the practitioner is to set about giving quinine. There are many ways of exhibiting the drug; however given, care must be taken that it is so administered that there can be no mistake about its being absorbed. If the patient for any reason, such as inability to swallow or persistent vomiting, cannot take quinine by the mouth, and the existing condition be grave, it may be injected by the rectum; but if the circumstances of the case are such that a rapid action of the drug is imperative, it must be injected at once intramuscularly, or into a vein.

When and in what dose to give quinine in ordinary cases.—During a paroxysm of ordinary intermittent fever it is better, before giving quinine, to wait until the rigor and hot stages are over and the patient is beginning to perspire. A fever fit, once begun, cannot be cut short by quinine, and to give quinine during the early stages aggravates the headache and general distress; but so soon as the skin is moist and the temperature begins to fall, the earlier the drug is commenced the better. Ten grains, preferably in solution, should be administered at the commencement of sweating, and thereafter five grains every six or eight hours for the next week. This is an almost certain cure. The quinine may not always prevent the next succeeding fit, but it

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nearly always diminishes its severity. In 99 cases out of 100 the second following attack does not develop.

When giving quinine it is well to administer an aperient and to keep the patient in bed; in ordinary cases neither aperient nor rest in bed is absolutely necessary. In cachectics, however, and in all obstinate cases, both are valuable adjuvants.

My practice in the treatment of ordinary malarial fevers is to give quinine for a week in the doses mentioned. At the same time, with a view to prevent recurrence of fever, I direct the patient, particularly if I have found the crescent form of the parasite in the blood—for such cases are specially prone to relapse—on one day a week (to give precision to my directions I generally mention Sunday), to take a mild saline, sulphate of soda or Carlsbad salts, in the morning, and three five-grain doses of quinine during the day, or fifteen grains in one dose. After the first week iron and arsenic in pill, tabloid or solution are prescribed for a fortnight, and, after an interval of a week, for another fortnight. The weekly aperient and quinine had better be kept up for six weeks or two months or longer.

Dose of quinine: toxic effects.—There is great difference of opinion and practice about the dose of quinine. Some give thirty grains at a dose, some give three. The former, in my opinion, is too large a dose for ordinary cases, the latter too small. It must never be lost sight of that occasionally quinine in large doses produces alarming effects; not singing of the ears and visual disturbances merely, but actual deafness and even amblyopia, both of which may prove very persistent and occasionally permanent. It may also produce profound cardiac depression and gastric disturbance, and even death from syncope. Urticaria is another, and not very uncommon effect of even small doses of quinine; some cannot take it on this account, and prefer to endure the disease rather than suffer the intolerable irritation induced by the remedy. I believe that nothing is gained by excessive doses; in ordinary circumstances, thirty

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grains spread over two or three days is usually ample to check an intermittent.

In the endemic area of hæmoglobinuric fever, and even in the case of individuals who have long left that endemic area, large doses of quinine do sometimes undoubtedly determine an explosion of that highly dangerous disease, especially so, but not exclusively so, in the cachectic. This important fact must not be lost sight of, and when there is any good reason to apprehend such a calamity, quinine should be given at first in one-grain doses gradually increased to five or more three or four times a day.

For children under one year, half to one grain for a dose suffices; for older children the dose must be increased proportionately to age and strength. Children tolerate the drug well, so that in serious cases—pernicious comatose or other cerebral forms—the drug should be vigorously pushed.

If a supposed ague resist the doses of quinine mentioned, the diagnosis should be revised.

Quinine in pregnancy.—Care should be exercised in giving quinine to pregnant females, for undoubtedly it sometimes causes miscarriage. The fact of pregnancy, however, must not debar the use of the drug altogether; only, in such circumstances, it should be given in the minimum dose likely to be effectual, say three grains repeated every eight hours for two days. A pregnant woman will run more risk of miscarriage and to her health from repeated ague fits than from a reasonable dose of quinine.

Quinine in the puerperal state.—It is a wise precaution in malarious countries to give a few five-grain doses of quinine during labour or soon after. The puerperal state seems to have the effect, as any other shock or physiological strain might, of waking up the slumbering malaria parasite. A dose or two of quinine in these circumstances does no harm, and may, by choking off a threatening fever, avert suffering and anxiety, not to mention danger.

Form in which to administer quinine.—Quinine is best given in solution, and probably the hydrochloride, as containing a larger proportion of the

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alkaloid than the sulphate, is the best salt. Some, under the impression that hydrobromic acid prevents the singing of the ears attending the free use of the drug, prefer this to dilute sulphuric acid as a solvent for the ordinary sulphate. When the tongue is fairly clean and digestion not altogether in abeyance, the quinine may be given in freshly prepared pill, in tabloid form, in cachet, or enclosed in cigarette paper; but in serious cases, particularly where the tongue is foul and digestion enfeebled, pills and tabloids are not to be trusted to. *In these circumstances they are apt to pass through the bowels and to appear in the bedpan unaltered.* In grave cases this occurrence must not be risked.

Euquinine or euchinine, the ethyl carbonate of quinine, is just as efficient as the other salts, and has the advantage of being tasteless, an important property in the case of fever in children or fanciful patients. I have made a considerable number of trials with this drug. It acts promptly on the fever, and causes the parasite to disappear from the blood.

Milk as a menstruum for quinine.—If the taste of the ordinary salts of quinine be very much objected to, and if euquinine is not available, a good plan is to give quinine in powder in a tablespoonful of milk after the patient has previously lubricated the mouth with a morsel of bread and butter. Given in this way the bitter taste of the drug is not perceived.

Hypodermic injection of quinine.—In any type of fever, if vomiting is persistent, if the brain is affected, or if the patient is insensible and cannot or will not swallow, recourse must be had to the hypodermic injection of quinine. In all cases in which life is in imminent danger, and in which the earliest possible action of the drug is of importance, it must be given hypodermically or, rather, intramuscularly. This method is sometimes a painful one, and may be attended with some risk of abscess; in the circumstances, such possibilities count for little. The most suitable readily procurable salt for hypodermic injection is the hydrochloride, or, better, the bi-hydrochloride, which is soluble in less than its own weight of water. The hydrobromide is equally soluble. If

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neither of these salts can be procured, the sulphate may be used, solution being effected by adding half its weight of tartaric acid.* Seven to fifteen grains dissolved in 30 to 60 minims of sterilised water would be a full hypodermic dose; in grave cases this dose should be given three times in the twenty-four hours. The needle should be driven well home, deep into the muscles of the gluteal or scapular region, the skin being previously carefully cleansed. The solution must be freshly prepared and boiled, and the syringe and needle thoroughly sterilised. A syringe, having a well-fitting glass piston and a plugging needle, has recently been put on the market; this is the best instrument for giving these injections. In the malignant fevers of Rome as much as a drachm of quinine, divided into three or four doses, is sometimes administered hypodermically in the course of twenty-four hours with the best results.†

The best place for a quinine injection is the gluteus maximus muscle at a point somewhere from

* The more serviceable salts of quinine, of which the bichloride of quinine and urea is one of the best, can now be procured in tabloid form specially prepared for hypodermic injection. These tabloids are much better than solutions, which cannot be kept for any length of time without risk of fouling.

† SOLUBILITY AND EQUIVALENT VALUE OF SALTS OF QUININE.

Those marked by an asterisk are suitable for hypodermic injections.

Name of Salt.	Percentage of the Alkaloid in the Salt.	Solubility in Cold Water.	Amount Equivalent in Value to One of Quinine Sulphate.
Sulphate	73·5 %	In 800 parts	1·00
Hydrochloride ...	81·8 %	,, 40 ,,	·9
*Bihydrochloride ...	72·0 %	,, 1 ,,	1·02
Hydrobromide ...	76·6 %	,, 45 ,,	·96
*Bihydrobromide ...	60·0 %	,, 7 ,,	1·23
Bisulphate	59·1 %	,, 11 ,,	1·24
Phosphate	76·2 %	,, 420 ,,	·96
Valerianate	73·0 %	,, 110 ,,	1·01
*Lactate	78·2 %	,, 10 ,,	·94
Salicylate	70·1 %	,, 225 ,,	1·05
*Hydrochloro-Sulphate	74·3 %	,, 2 ,,	·99
Arseniate	69·4 %	slightly soluble	1·06
Tannate	20·0 %	,, ,,	3·67
*Bichl. of Q. and Urea			

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two to three inches below the crest of the ilium. After the injection is made the part should be gently massaged so as to diffuse the solution, and the little wound sealed with collodion. Quinine ought never to be injected into the neighbourhood of large nerves or blood-vessels, and never into the subcutaneous connective tissue as in the case of morphia and other alkaloids. I have long been in the habit of using intramuscular injections of quinine both in hospital and in private practice, and, so far, without mishap. My belief is that abscess, indurations, and similar accidents are attributable to imperfect methods and carelessness.

Intramuscular injections of quinine, 7 to 10 grains daily for a week, is the best way of checking obstinately relapsing malarial attacks.

Precautions.—It may be well to mention, not with the idea of deterring the practitioner from using the drug in this way, but to impress upon him the necessity for care in keeping instruments and solutions aseptic, that not only abscess, sloughing, and chronic painful indurations have sometimes followed the hypodermic injection of quinine, but also tetanus. In these latter unfortunate cases it was not the quinine that caused the tetanus; it was the tetanus bacillus, and this tetanus bacillus was introduced either on a dirty needle or in a fouled solution. Tetanus is an exceedingly common disease in some tropical countries. In Western Africa, for example, a large proportion of wounds, no matter how trifling as wounds they may be, if they are fouled by earth or dirt result in tetanus. The French in Senegambia have found this to their cost. A gentleman who had travelled much in Congoland told me that certain tribes poison their arrows by simply dipping the tips in a particular kind of mud. A wound from these arrows is nearly sure to cause tetanus. In many tropical countries, so general and so extensive is the distribution of the tetanus bacillus that trismus neonatorum is a principal cause of the excessive infant mortality. Every precaution must therefore be taken to ensure that the little instrument which is so potent in saving

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life may not by carelessness be turned into an instrument of death.

Quinine by enema.—Quinine may also be given by enema. It is readily absorbed if the bowel be not too irritable. The dose should be a large one. Thirty grains given in this way to a child in malarial comatose fever has sometimes a rapid effect.

Intravenous injection of quinine.—In cases of pernicious comatose remittent, in which it is of importance to obtain a rapid and powerful action of the drug, Bacelli recommends the intravenous injection of the following solution: Hydrochloride of quinine 1 gramme, sodium chloride 75 centigrammes, distilled water 10 grammes. This solution he has employed in these desperate cases with much success, injecting directly into a vein 5 to 7 grammes at a time; he states that whereas with hypodermic injection the mortality in such cases amounted to 17 per cent., with intravenous injection it was reduced to 6 per cent.

Warburg's tincture.—A very effective medium for giving quinine, and one of high repute in many places, is Warburg's tincture. This contains, besides quinine, a number of drugs, many of them doubtless inert, although some of them certainly possess valuable therapeutic properties. Experience has shown that the combination is really a good one, and that Warburg's tincture sometimes succeeds where quinine alone fails, or acts too slowly. It generally proves a powerful sudorific. The dose is half an ounce, and is repeated after two or three hours. The action appears to be somewhat similar to that of the antipyretics now in vogue—antipyrin, phenacetin, etc.—drugs which, when given in combination with quinine in the routine treatment of malarial fevers, although they have no curative properties, sometimes contribute very markedly to the relief of headache and febrile distress. They must be used with great caution in adynamic cases. At the present time these drugs are much abused in many malarial countries.

Mode of action of quinine.—In what way quinine acts has not yet been satisfactorily explained.

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Some, reasoning from the toxic influence this drug exerts on many kinds of free amœbæ, say that it acts in malaria in the same way—that is, as a direct poison to the parasite. They support this view by pointing to the degenerative changes, as evidenced by imperfect staining reaction, exhibited by such parasites as persist in the blood after administration of quinine has been commenced. Others maintain that it acts in stimulating the phagocytes, the natural enemies of the parasite. Some experimentalists allege, on the other hand, that it paralyses the white corpuscles. That quinine does not kill all blood protozoa is certain, for it has no effect on the hæmoprotozoa of birds and reptiles, or on the trypanosomes. Certain it is that in man, with the exception of the crescent body, it usually quickly causes the parasite to disappear from the general circulation. It is said by some to be most effective against the free spores and the very young intracorpuscular forms, but inoperative against the more mature parasites; hence they advocate giving it early in the parasitic cycle. Others, on the contrary, maintain that it is operative only on the large intracorpuscular forms, and therefore advocate its use at a late stage of the cycle.

Strange to say, quinine, especially in small doses, seems sometimes to wake up latent malaria and to bring about an ague fit. The same may be said of a course of mineral waters, of hydropathic treatment, and of sea-bathing.

Treatment of bilious remittent.—In bilious remittent and other severe forms of malarial fever one must not, as in a simple intermittent, wait for the remission before giving quinine. To wait for remission or sweating used to be the practice; it was said that to give quinine at any other time was wrong, and that something terrible would happen if the superstition were ignored. *In all grave fevers a full dose, ten or fifteen grains, should be administered at once.* The parasite cannot be attacked too soon. It is desirable to have the bowels freely opened; quinine is said to act better then. It is a mistake, however, to delay the administration of

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the specific pending the action of the aperient. If an aperient be indicated, it should be given along with the quinine. Five or ten grains of calomel is the best. Thereafter the quinine, in five-grain doses, should be repeated every three or six hours until fever has subsided. If there be much bilious vomiting, an emetic of ipecac. or repeated draughts of hot water will clear the stomach and perhaps, after a time, enable it to retain the quinine. The drug is sometimes more readily retained if given in chloroform water or in effervescing form. Mustard poultices to the epigastrium, small hypodermic injections of morphia, ice pills, sips of very hot water, effervescing mixtures, champagne, one- or two-drop doses of tincture of iodine, are each of them, on occasion, aids in stopping vomiting. If these measures fail, and if the vomiting is so frequent and so severe that the dose is immediately rejected, and if there is no diarrhœa, it is advisable to clear out the rectum with an injection of warm water and, when the action of this has concluded, to throw up an enema of thirty grains of quinine in three to ten ounces of water with a few drops of acid to aid solution; at the same time, five or ten grains of calomel may be given by the mouth. This failing, or in preference to this, recourse must be had at once to intramuscular injections. So soon as the stomach has quieted down, quinine may be given again by the mouth.

Treatment of hyperpyrexia.—Hyperpyrexia must be promptly met by prolonged immersion in the cold bath, rectal injections of iced water, ice bags to the head, etc. At the same time quinine must be injected intramuscularly, or into a vein, in full doses, and repeated every three hours until thirty or forty grains have been given. Prompt action in these cases is of the first importance, and may save life. If temperature be kept down for three or four hours the quinine gets time to act on the parasites crowding the intracranial vessels; but if temperature be allowed to mount and to remain high the patient is destroyed before the specific has a chance. The cold bath, therefore, is absolutely necessary. In such circumstances,

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antipyrin and similar antipyretics are worse than useless. Good rules are to prepare to give the cold bath if the axillary temperature reach 106°, and to remove from the bath when rectal temperature has fallen to 102° Fahr. Although the temperature has been reduced by this means, thermometrical observations must be continued at short intervals, say every two hours; directly it begins to rise again, say to 102°–103°, the patient should be replaced in the bath; this must be repeated as often as necessary. Patients who have suffered from a hyperpyrexial attack should be invalided home.

Treatment of algide and dysenteric attacks. — Algide and dysenteric attacks demand quinine combined with a little opium. If dysenteric symptoms persist, ipecac., or the aperient sulphates in full doses and opium must also be given.

Other drugs in malaria.—During the continuation of a fever I have never seen much, if any, good from arsenic. The place of arsenic is not as a substitute for quinine during fever, but as a blood restorer after fever. I have heard of cases of obstinate ague cured by half-drachm doses of liquor arsenicalis. I have never myself ventured on these heroic doses. A strong infusion of "the hairs that grow between the grain and the outer leaves of the mealie cob" (dose, three tablespoonsfuls) has recently been recommended as a cure for malaria; I have no experience of it. I have never seen benefit, in any way approaching that derived from quinine, from methylene blue, carbolic acid, iodine, anarcotine, analgen, phenocol, parthenium, ailanthus, chiretta, eucalyptus, or any of the many drugs which from time to time have, on very limited experience, been recommended in malaria. In those cases, however, in which from some idiosyncrasy the patient is unable to take quinine, it may be necessary to have recourse to some of these drugs. Methylene blue in doses of two to three grains, and pushed until the urine becomes deeply tinged or signs of kidney irritation appear, enjoys a certain reputation in America and in Germany. Anarcotine was at one time, during a

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quinine famine, extensively and successfully employed in India; the dose is from one to three grains. Phenocol hydrochloride, in ten-grain doses, administered five, three, and two hours before the expected paroxysm, has been used with advantage in Italy, and is said to have succeeded in some instances in which quinine had failed. Tannin has been recommended in obstinate cases where quinine had failed or could not be taken. A grain of capsicum with five grains of quinine is said to succeed sometimes where quinine alone fails. I have given this pill, but cannot determine how much the capsicum contributed to the cure. I cannot say I have ever seen an ordinary uncomplicated ague absolutely resist quinine properly given. I have seen cases of obstinately recurring ague apparently permanently cured by a few hypodermic injections of quinine, although the same drug, given in the ordinary way, had proved a comparative failure. There can be little doubt, however, that in rare cases it does fail, and that it is more efficient against the benign tertian and the quartan than against the malignant parasites. It does not always prevent relapse, even in the non-malignant infections.

Treatment of splenic tumour and malarial cachexia.—The enlarged spleen of malarial cachexia is best treated by counter-irritation (linimentum iodi, or ung. hydrarg. biniodid.) and saline aperients, combined with quinine, arsenic, and iron. Hepatic enlargement and abdominal congestion arising from malarial disease of long standing generally derive much benefit from a course of Harrogate, of Kissingen, of Carlsbad, or of other aperient mineral water. When these waters cannot be obtained, a morning aperient saline, kept up for two or three weeks, is an efficient substitute. Aperient courses should, as a rule, be combined with moderate doses of quinine, and be followed by courses of iron and arsenic. Cachectics should leave the malarial centre where they are being poisoned and spend at least one year in Europe. They must be careful to clothe warmly, especially on first entering colder latitudes; to keep lightly employed both in body and mind; to avoid over-fatigue, con-

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stipation, exposure to a very hot sun, high winds, rain ; to live temperately, and generally to follow the dictates of common sense. Residence in a dry, cool, sunny climate, or a sea voyage, is an admirable restorative in malarial cachexia.

Malarial cachectics must exercise great caution about exposing themselves to the fresh sea breezes on the return voyage to Europe. Neglect of this is nearly sure to be punished with an attack of fever, sometimes of fatal blackwater fever. Many such fatalities occur yearly in cachectics from West Africa during the voyage to Europe. Return to Europe in the winter season should, if possible, be avoided, the colder months being spent in the Canaries, Egypt, or the Riviera. *If quinine is being taken when the patient leaves for Europe, its use, in the accustomed dose, should be systematically continued during the voyage and for several months, at least three, after arrival.* I find that malarial cachectics are often allowed to start on the voyage to Europe inadequately instructed on these important points.

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Food and drink in malaria.—The food in malarial fevers ought to be light and principally fluid. Effervescing mixture often helps to clean the tongue and settle the stomach. Lemon decoction (made by boiling for half an hour a sliced lemon, including skin and seeds, in a pint and a half of water, straining, diluting, and sweetening) is much relished in remittents, and may be taken systematically by all malarials with advantage. Fresh lemonade, fresh lime juice, weak cold tea, and iced water sipped, are all of them much appreciated by these patients. During convalescence the quality of the food should be gradually improved and, if necessary, supplemented by a light wine or bitter ale.

PROPHYLAXIS.

The basis of malaria prophylaxis is the fact that particular species of mosquitoes are indispensable for the propagation of the parasites. Practical measures, therefore, have for their object the extermination of these insects, or, failing this, the prevention of their

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bites. War need not be waged against all mosquitoes; our present knowledge seems to indicate that only the *Anophelinæ* have to be considered. As the members of this sub-family are easily recognised (p. 144), and as they are somewhat fastidious in their habits, their extermination in limited areas is by no means a hopeless task.

Drainage, cultivation and flooding.—Experience has shown that much can be done to free a locality of malaria. Drainage and cultivation where the land will repay the expenditure, permanent and complete flooding where it will not and where such flooding is possible, proper paving and draining of unhealthy towns, and the filling in of stagnant, swampy pools—these are the more important things to be striven for in attempting the permanent sanitation of malarious districts. In England, in Holland, in France, in Algeria, in America, and in many other places, enormous tracts of country which formerly were useless and pestilential have been rendered healthy and productive by such means.

In carrying out extensive public works care should be exercised to provide good subsoil drainage in connection with irrigation, to provide efficient drainage to carry off superfluous water *before* introducing a larger water supply into a town previously inadequately watered, and to avoid interfering with the natural drainage of a district in constructing railways and so forth. To do anything that may raise the level of the subsoil water in potentially malarial districts is most dangerous. Equally so is the neglect to fill up, or provide for the drainage of excavations, such as the "borrow-pits" in railway construction or similar holes in which rain water may accumulate and create breeding pools for mosquitoes.

Location of dwelling-houses. — The inhabitants of malarious districts ought to live in villages or towns with well-paved streets and courts, going out to cultivate their fields during the day, but returning to sleep in the town before nightfall. Houses should be placed, if possible, on high and dry situations, a clay soil being avoided. It is unwise in

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countries such as Africa, where nearly all Europeans suffer from chronic malarial poisoning, to place dwelling-houses in exposed situations, or where high winds are apt to produce chills and consequent fever relapses. For the same reason, in elevated situations houses should be well sheltered by trees planted at some distance from the premises, or by higher ground. In the neighbourhood of houses the felting of natural grass should, if possible, be preserved, or, if it be disturbed, replaced immediately, or the exposed soil covered with rammed clay or cement. It is unwise to have flower-beds or vegetable gardens near bedroom windows, or to allow water from bath-rooms or cook-houses to flow over the ground in the vicinity of the house, or to keep water unchanged in tubs or water-butts for mosquitoes to breed in. Pools and puddles of stagnant water should be filled up and turfed. Ponds should be stocked with fish, as fish tend to keep down mosquitoes by preying on their larvæ. The neighbourhood of swamps is to be avoided. A few ounces of petroleum thrown on the surface of a pond will prevent mosquitoes from depositing their eggs on the water, and will asphyxiate their larvæ; the petroleum requires to be renewed from time to time—say once a week. Coal tar may be used in the same way. There are many simple precautions of this sort which will occur to every prudent man, and which, in malarious countries, he should take care to have carried out.

Danger from vicinity of natives.—Seeing that a large proportion of the native children harbour the malaria parasite, and that a large proportion of the anophelines in the neighbourhood of native houses are infected, it is manifest that to visit native quarters when mosquitoes are feeding, especially in the evening or during the night, is fraught with danger. For the same reason the European should build his house or pitch his camp well away from native quarters, and beyond the flight of infected anopheles; and, for the same reason, native children should not be allowed to frequent Europeans' establishments.

The cultivation of trees and plants.—

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Much was expected at one time from the cultivation of eucalypti of different species—particularly *Eucalyptus globulus*—as a means of suppressing malaria. Specific virtues were attributed to its balsamic exhalations. These hopes have not been fulfilled in every case; but, undoubtedly, the effect of this rapidly-growing tree in drying the soil is of use in some localities. The same may be said of the cultivation of the sunflower, chrysanthemum, kiri tree, and other plants. Possibly these plants influence insect life in other ways.

Native experience to be consulted.—It is unwise to build where the natives say the neighbourhood is unhealthy; natives generally know such places. Neither, if it can be possibly avoided, should a stay be made where the natives are anæmic and have enlarged spleens—a sure indication of an unhealthy district.

Other precautions.—Bedrooms should be situated in an upper storey, and dwelling-rooms be well raised on piles or arches above the ground. Common sense tells us that campaigns and journeys in malarious districts should be conducted and concluded during the healthy season, if there be one. *Mosquito nets must invariably be used;* many travellers attest their value, so plainly indicated by recent discoveries. The body should be covered up during sleep, and every precaution (as fires, etc.) that circumstances permit should be employed to keep mosquitoes away.

The subjects of malarial infection are dangerous to their companions; they should, therefore, be avoided or, if this is impracticable, compelled to sleep under efficient mosquito nets. Mosquitoes must be rigorously excluded from hospitals. It will prove a truly economical procedure to supply natives liberally with quinine; this should go hand in hand with other steps that may be taken to render a place salubrious.

Mosquito-protected houses.—It has been proved experimentally and practically that complete protection from mosquito bite, and therefore from malaria, can be secured by having the dwelling-house

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protected by gauze fittings, with a mesh not larger than twelve strands to the inch, in the doors, windows, chimneys, and ventilators. When possible, such measures should be adopted and intelligently applied. I believe some such arrangement will, in the near future, be a feature in the domestic architecture of malarial countries.

Quinine and arsenic as prophylactics.—A great deal has been written about the prophylactic use of arsenic and quinine in malaria. Opinions are very much divided on the subject. Most deny that arsenic possesses any prophylactic power whatever. Duncan, after an exhaustive study of the recorded evidences, and after extensive and carefully conducted experiments made by himself on large bodies of troops, concludes that arsenic has no prophylactic virtue whatever; but that quinine, in a daily dose of three to five grains, lessens the fever admissions by one-half. He therefore strongly advocates the systematic use of the latter drug in all campaigns involving a sojourn in malarious districts. In this he is backed by the opinion of many medical men of experience. Corre, although he admits the prophylactic power of quinine against ordinary malarial fever, says it has no influence in preventing pernicious fevers. Other authorities, on the contrary, state that those who take quinine systematically, though liable to mild fevers to some extent, enjoy immunity from pernicious attacks. On the whole, the evidence is distinctly in favour of the systematic employment of a dose of quinine as a prophylactic.

There is considerable difference of opinion and practice as to the dose and the time of administration of quinine. There are three principal methods:—(*a*) five grains every day after breakfast, (*b*) ten grains twice a week, (*c*) fifteen grains every tenth and eleventh day. Some prefer one method, others another; when one plan proves unsatisfactory another should be tried. If for any reason quinine is not tolerated, that individual is unsuitable for residence in malarious countries.

Other prophylactics.—Tea, coffee, and very

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small doses of alcohol are also decidedly of service; but they should be used in strict moderation, the last being taken only after the work of the day is over, and when there is no longer any necessity for going out in the sun. Crudeli speaks highly of lemon decoction (made as already described, page 128) as a prophylactic; its use can do no harm, and it is a pleasant, slightly tonic, and slightly aperient beverage, well suited as a drink in hot climates. The decoction made from one lemon may be taken daily in divided doses.

Education.—It is impossible to lay down directions for the prevention or suppression of malaria which would be applicable at all times and to all places, and under every circumstance. What might suit one set of conditions might not be appropriate in other conditions. But by one, or other, or all of the measures indicated above, much can be done to mitigate or avoid endemic malaria. Perhaps the most important initial measure in the struggle with the pestilence is the education of the inhabitants of malarial countries in the mosquito-malaria theory. Sanitary measures can rarely be carried out effectually without the co-operation of those whom they are intended to benefit; and this co-operation cannot be secured unless the rationale of their operation is understood. Therefore, those responsible for the public health in malarial districts should, by one means or another, indoctrinate the people in the mosquito-malaria theory. If he succeed in this, the sanitarian will have an easier and a more hopeful task.

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CHAPTER IX

MALARIA: THE MOSQUITO

THE part played by the female mosquito, or gnat, in the life-history of the germ of malaria, as well as in that of yellow fever, of filariasis, and, most probably, of other diseases of warm climates, renders some knowledge of the natural history of this insect a necessity for the tropical pathologist.

Although the *Culicidæ* or mosquitoes had received, now and again, some attention from naturalists ever since the time of Linnæus, it is but recently that the extent, complexity, and importance of this group of insects have been apprehended. Considerations of space preclude me from giving more than the merest outline of the subject; those who desire to follow it up would do well to provide themselves with one, or more, of three recent works—namely, Theobald's *Monograph of the Culicidæ*, Blanchard's *Les moustiques*, Giles's *Handbook of the Gnats or Mosquitoes*, in which will be found details of all that was known about these insects up to the date of their publication.

The **Culicidæ**, of which there are at least 500 known and, probably, over 200 additional and as yet undescribed species, belong to the order of *Diptera*, or two-winged insects, in which the posterior of the two pairs of wings of the typical insect are rudimentary, being represented by the *halteres* or balancers (Fig. 26). Like the other members of the order, they lay *eggs*, from which is hatched a worm-like *larva*, which, after growth and several changes of skin, ceases to eat, and becomes converted into a *nymph* or *pupa*, from which, by a rupture of the pupa-case, the adult insect or *imago* emerges.

The geographical range of the mosquito extends from the frigid zones to the equator. Given stagnant or slow-flowing water and a summer temperature,

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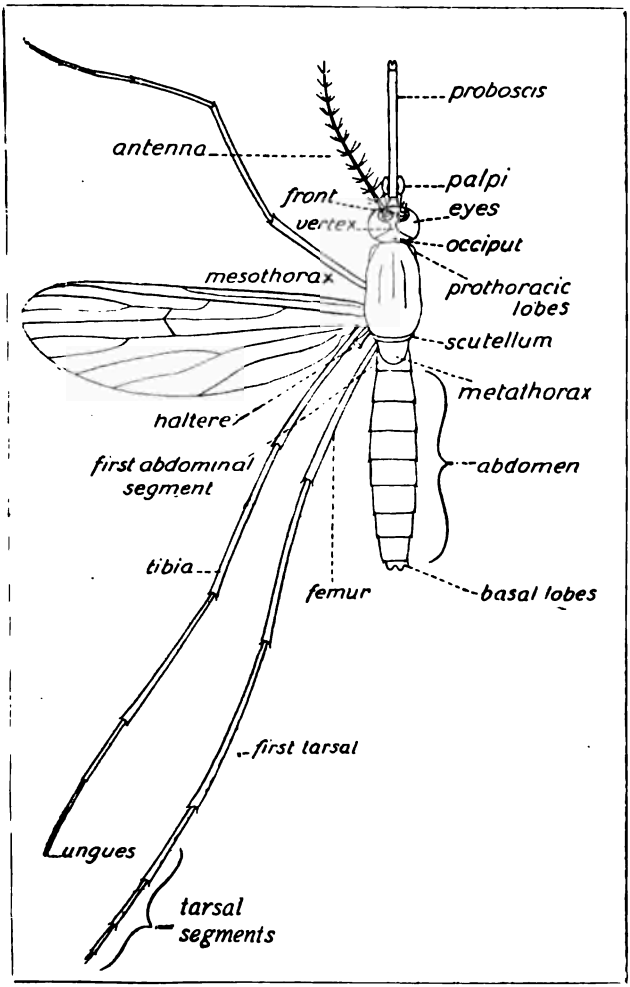

Fig. 26.—Female Mosquito.

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there this family of insects will be represented by one or many species. The distribution of particular species and the abundance of mosquitoes in any given place are determined, in addition to temperature and hydraulic conditions, by complicated circumstances not yet wholly understood.

The adult insect feeds on vegetable juices, the males, with few exceptions, exclusively so. In addition to a vegetable diet, the females of most species, when opportunity offers, suck the blood of mammals, birds, occasionally of fishes, reptiles, and even that of other insects and their larvæ. The male mosquito, not being a blood sucker, takes no part in

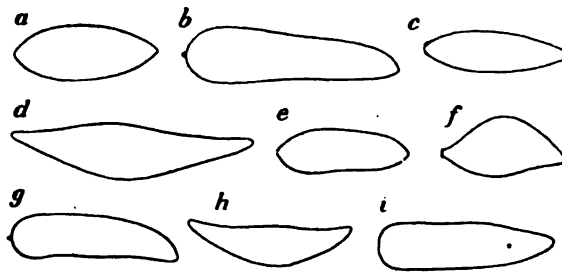

Fig. 27.—Various forms of mosquito eggs.

a, Grabhamia dorsalis; *b*, Culex pipiens; *c*, Culex scapularis; *d*, Mansonia titillans; *e*, Stegomyia fasciata; *f*, Tæniorhynchus fulvus; *g*, Culex fatigans; *h*, Ianthinosoma mexicanum; *i*, Tæniorhynchus fasciolatus.

the diffusion of disease; it is the female only that is a germ carrier. Soon after impregnation the female lays her eggs (Figs. 27, 28, 29) from time to time—singly, in groups, or in boat-shaped masses, according to species—on the surface of still water, on which they float. The process of hatching out depends in great measure, as indeed do all the developmental processes connected with the mosquito, on temperature, being retarded or even suspended by cold and accelerated by warmth. At ordinary summer temperature the larvæ hatch out in from two to three days, and at once proceed to feed voraciously on the organic materials

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suspended in the water. Being air-breathers, a great part of their time is passed at the surface of the water, where they lie in such a position —which varies with species—that the respiratory opening placed near the tail can function readily (Figs. 30, 31). After the several moultings the larva, now very much increased in size, passes to the nymph or pupa phase (Fig. 32), during which the little animal ceases to feed, and for the most part floats just awash at the surface of the water. In from one to two days the pupa-case bursts and the insect, emerging, stands on the empty case till its wings have dried, when it flies away. From first to last, from egg to imago, the process of development takes about a month in the temperature of the Italian summer. As each female mosquito may

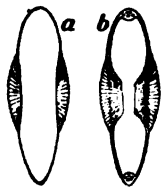

Fig. 28.—Eggs of Anopheles maculipennis.
a, Under side; *b*, upper side.

Fig. 29.—Culex pipiens—egg-boat.
(*After Sambon.*)

lay eggs many times in a season, and many hundreds of eggs each time, and as the young female can produce eggs within a week or ten days after her emergence from the pupa-case, it follows that one pair of insects can give rise to several millions of their kind in the course of a summer.

During cold weather the development of the larva is temporarily suspended, and the surviving adults, at all events the females, hibernate in dark and sheltered places, to become active again on the return of warm weather. In this way, and as larvæ, the species is carried over the cold weather of winter. The duration of the life of the adult insect has not been definitely ascertained; it is known that some species, if supplied with water and suitable food, can live for several months.

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It is suggested that the mosquito tends to return to the particular pool in which she herself was hatched out to deposit her own eggs, and that she rarely

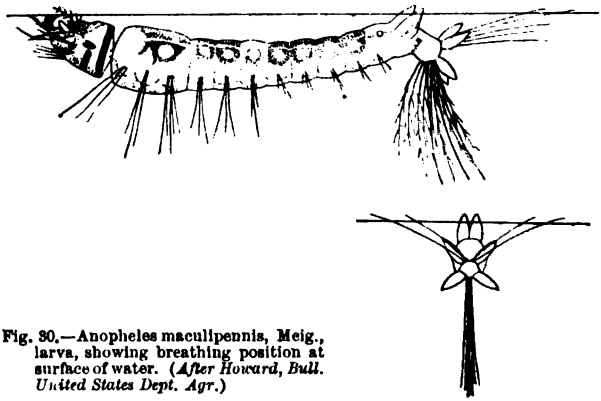

Fig. 30.—Anopheles maculipennis, Meig., larva, showing breathing position at surface of water. (*After Howard, Bull. United States Dept. Agr.*)

strays from the vicinity more than a few yards, quite exceptionally beyond half a mile. Occasionally she may be blown for some distance by

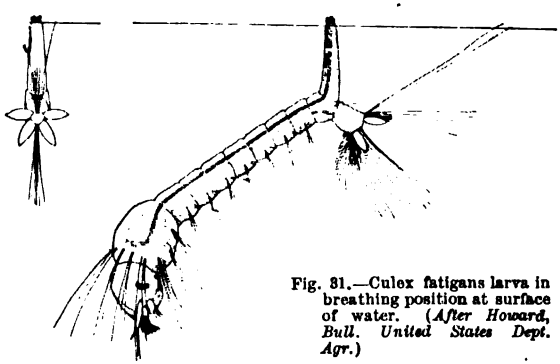

Fig. 31.—Culex fatigans larva in breathing position at surface of water. (*After Howard, Bull. United States Dept. Agr.*)

gentle winds; and it is believed that under certain circumstances, probably connected with food-supply and over-stocking, she will travel singly or in vast swarms for long distances. Such migrations, however,

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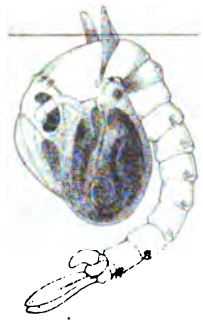
are quite unusual. Of course, mosquitoes may be, and often are, transported great distances in ships, railway carriages, and similar vehicles, and in this way man aids in their diffusion; but for the most part the mosquito is a feeble and timid flier, disliking to leave her accustomed haunt, and seldom rising high above the ground. So soon as even a moderate breeze springs up she seeks shelter in bush, or house, or cranny. Some species are domestic; others live exclusively in jungle or forest; some, after passing the day in the open, visit human habitations, or the haunts of birds and beasts, during the night. The

Pupa of Anopheles maculipennis.



Pupa of Culex fatigans.

Fig. 32.

great majority of species are nocturnal in habit, although many of these can be coaxed into activity by the reproduction of night-like conditions of shade and atmospheric stillness.

The accompanying figures (Figs. 26–40) give a good idea of the leading features of the anatomy of the mosquito and of the names applied to the various parts and organs, and will help the student to understand descriptions of genera and species.

The antennæ of the male insect (Fig. 33, *a*, 33A, *c*) are adorned with a profusion of long silky hairs, in marked contrast to the scanty, down-like and short hairs on the antennæ of the female; this is an easily recognised indication of sex.

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The proboscis consists of a number of piercing elements enclosed in a sheath—the labium, which, at

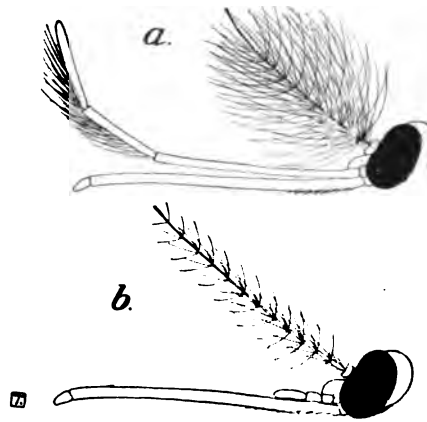

Fig. 33.—Heads of Culicinæ.
a, Male; *b*, female.

its free end, is tipped with two minute labella. In feeding, the mosquito raises her hind legs and presses the tip of the proboscis against the skin. This

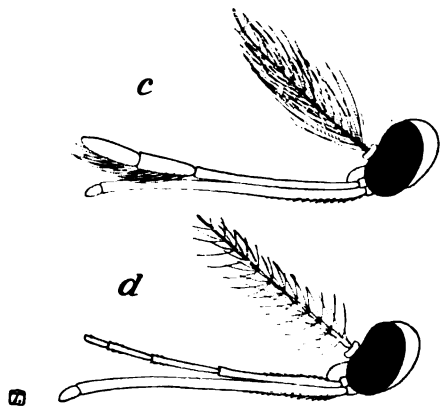

Fig. 33A.—Heads of Anophelinæ.
c, Male; *d*, female.

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causes the labella (Fig. 34, *h*) to splay out and so serve as a support to the piercing elements—namely, the labrum, hypopharynx, mandibles, and maxillæ (Figs. 34, 35)—which are now thrust into the skin. The labium does not penetrate; as the stabbing elements sink into the skin it bends backwards about its middle, the labella still pressing against the skin and clasping the stilettes. The secretion of the salivary glands (Figs. 10, 13) passes along the salivary duct and thence down a minute canal which traverses the hypopharynx to its tip, and so into the subcutaneous tissues of the bitten animal. It is supposed

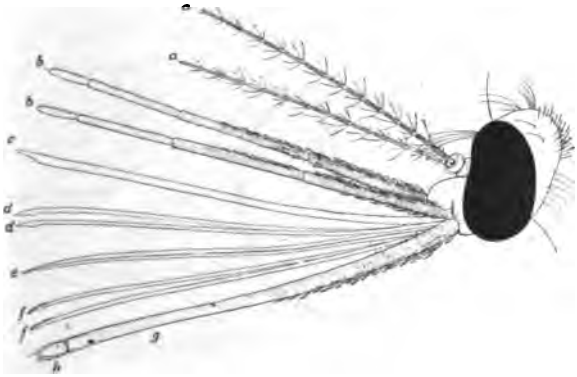

Fig. 34.—Mouth parts of female mosquito.
a, *a*, antennæ; *b*, *b*, palpi; *c*, labrum-epipharynx; *d*, *d*, mandibles; *e*, hypopharynx; *f*, *f*, maxillæ; *g*, labium; *h*, labella.

that the function of this secretion is, by irritating, to determine a flow of blood to the part bitten, and also to prevent coagulation of the blood. To many people this secretion is a powerful irritant, although repeated inoculation tends to produce tolerance, as in the case of many other organic poisons.

A buccal tube is formed by the apposition of the upper surface of the hypopharynx to the under surface of the labrum (Fig. 35). Along the tube so formed the blood is aspirated by the expansion of the gizzard-like organ (Fig. 10, *b*), and then driven by the contraction of the same into the stomach

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(Fig. 10), or middle intestine, as it is called. A mosquito will fill herself in a minute or thereabouts. She then withdraws her proboscis and flies heavily away to some sheltered spot to digest the meal. Apparently the first step in digestion is the concentration of the blood she has imbibed; this is effected by excretion of the watery portion of the liquor sanguinis. Often while this process of dehydration is proceeding, even while she is sucking, droplets of clear fluid may be seen ejected at her anus. The concentrated blood becomes in this way a viscid tarry mass, which is gradually, in the course of three or four days, partly absorbed and partly voided as gamboge-coloured fæces. The mosquito is now ready for another meal.

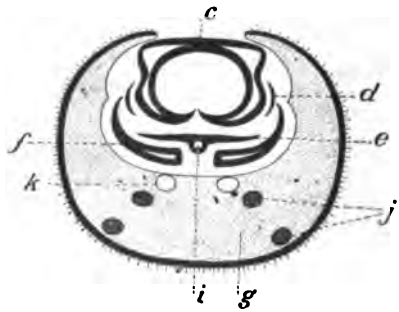

Fig. 35.—Section of mosquito. (*Adapted from Nuttall and Shipley.*)
c, Labrum-epipharynx; *d*, mandibles; *e*, hypopharynx; *f*, maxillæ; *g*, labium; *i*, salivary duct; *j*, muscles; *k*, tracheæ.

The rich pabulum supplied by blood seems to favour ovulation.

Diagnosis. — Many kinds of insects possess blood-sucking propensities. As a rule there is little difficulty in distinguishing most of these from the mosquito. There are certain *Diptera*, however, which closely resemble the latter in appearance as well as in habit. These the student should learn to distinguish.

The principal of the mosquito-like blood suckers are the Midges (*Cheironomidæ*) and the Sandflies (*Simulidæ*). The following are the diagnostic points:—

Mosquitoes have a long suctorial proboscis, and the veins of their wings are fringed with scales.

Midges are very slender and minute, have a short

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suctorial apparatus, and narrow wings without scales.

Sandflies are small, obese, and hump-backed, have short suctorial apparatus, comparatively stout legs, broad wings, and short, curved, hairless antennæ.

It is desirable that the medical man should be able not only to recognise mosquitoes but also to determine genera and species. Obviously, it would be impossible to give in a concise manual on tropical diseases minute descriptions of the vast number of species already described. Moreover, the classification of these insects is still very unsatisfactory. I must, therefore, refer the reader to the monographs

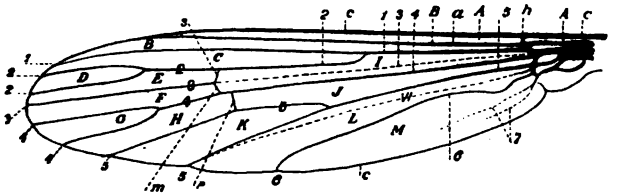

Fig. 86.—Wing of Culex concolor (male), to illustrate terminology.

c, costa; *a*, auxiliary vein; *1–6*, first to sixth longitudinal veins and branches; *7*, seventh or false (unscaled) longitudinal vein; *VI*, unscaled vein between fifth and sixth longitudinal veins; *h*, humeral transverse vein; *s*, supernumerary transverse vein; *m*, middle tranverse vein; *p*, posterior transverse vein; *A*, costal cells; *B*, subcostal cells; *C*, marginal cell; *D*, anterior fork cell or first submarginal cell; *E*, second submarginal cell; *F*, first posterior cell; *G*, hindar fork or second posterior cell; *H*, third posterior cell; *I*, first basal cell; *J*, second basal cell; *K*, anal cell; *L*, axillary cell; *M*, spurious cell.

on the subject already mentioned. On the next page I give a **synoptical table** which will enable the student to identify the main groups or sub-families to which any given mosquito belongs. It has been prepared after a careful consideration of the various classifications proposed. This table is followed by Theobald's classification of the Anophelinæ, to which group, so far as we know at present, the malaria-bearing mosquitoes are restricted. (*See* p. 145.)

Theobald divides the Anophelinæ into eighteen genera, which he distinguishes by the shape and arrangement of the scales. I will not discuss the value of this classification, but I must remark that many authorities regard the characters given by

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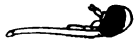
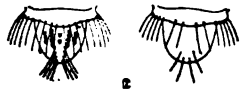
FAMILY CULICIDÆ*—Classification of Sub-Families.

Proboscis.	Straight 	*Metanotum.* Nude	*Palpi.*	Long in ♀ and ♂	— *Scutellum* simple, never trilobed	*Anophelinæ* (1), Theobald.
				Short in ♀ and ♂	*Wings.* 1st sub-marginal cell equal to or longer than 2nd posterior cell	*Ædinæ* (2), Theobald.
					Wings. 1st sub-marginal cell shorter than 2nd posterior cell. Both very small	*Uranotaeninæ*, Mitchell.
				Short in ♀ long in ♂	*Wings.* Six long scaled veins	*Culicinæ* (3), Theobald.
					Wings. Seven long scaled veins	*Heptaphlebomyinæ*, Theobald.
		With scales or hairs 	*Palpi.*	Short in ♀ and ♂		*Dendromyinæ*, Lutz
				Short in ♀ long in ♂		*Joblotinæ* (4), Blanchard.
	Recurved	*Palpi* long in ♂; long or short in ♀				*Megarhininæ* (5), Theobald.

* The *Corethrinæ* hitherto included in this family were separated and raised to the rank of a family (*Corethridæ*) by Eysell in 1905. They differ greatly from the *Culicidæ* by the structure of the mouth, which is not formed for piercing, by the absence of scales on wings, and many other peculiarities.

Synonyms.—(1) *Anophelina*, Theobald. (2) *Ædeimyina*, Theobald. (3) *Culicina*, Theobald. (4) *Trichoprosoponinæ*, Theobald, *Hyloconopinæ*, Lutz. (5) *Lynchinellinæ*, Lahille.

OTHER SUB-FAMILIES PROPOSED.—Mitchell proposes the formation of a new sub-family *Deinoceratinæ*, to include *Ædinæ*, with very long second antennal joints. Theobald suggests a new sub-family *Limatinæ* for those *Dendromyinæ* in which the males have a jointed proboscis bent above the middle of its course. Christophers proposes to raise the genus *Stegomyia*, belonging to the Culicinæ, to the rank of a sub-family.

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Generic Classification of Sub-Family Anophelinæ, adapted from Theobald.

- *First sub-marginal cell of wing.*
  - Large
    - *Joints of Antennæ.*
      - With many dense scale tufts . . . . . *Chagasia.*
      - Without dense lateral scale tufts
        - *Thorax* / *Abdomen* — Hair-like curved scales
          - *Head scales.* — Upright forked
            - *Basal lobe of genitalia.*
              - 1 Segment
                - *Wing scales.* — Large, lanceolate . . *Anopheles.*
                - *Wing scales.* — Mostly small, long, and narrow, or slightly lanceolate . . *Myzomyia.*
                - *Wing scales.* — Large, inflated, and disposed in patches . . . . *Cycloleppteron.*
              - 2 Segments — *Prothoracic lobes* with dense outstanding scales . . *Peltinella.*
          - Some flat in median area — *Prothoracic lobes* mammillated. *Wing scales* lanceolate . . . . . *Stethomyia.*
        - *Thorax* — With narrow curved scales; *Abdomen* — Hairy
          - *Head scales.* — Normal, forked. *Wing scales* small lanceolate . *Pyretophorus.*
          - *Head scales.* — Broad, not closely oppressed, but not forked or fimbriated. *Wing scales* broad, lanceolate . . . . . *Myzorhynchella.*
        - *Thorax* — Hair-like curved scales—some narrow curved scales in front; *Abdomen* — Hairy on dorsal surface—scaly on venter—prominent apical lateral scale tufts—no ventral tuft; *Wings* — Scales lanceolate . . . *Arribalzagia.*
        - *Thorax* — Hair-like curved scales; *Abdomen* — No lateral tufts—a distinct apical tuft; *Palpi* densely scaly. *Wings* with dense large lanceolate scales . . . *Myzorhynchus.*
        - *Thorax* — Hair-like curved scales, and some narrow-curved lateral ones; *Abdomen* — Hairy with dense hair-like lateral apical scaly tufts; *Wings* — With scales short, dense, lanceolate. *Fork cells* short . . . . . *Christya.*
        - *Thorax* — Very long hair-like curved scales; *Abdomen* — Hairy, last two segments scaly; *Wings* with broadish, blunt, lanceolate scales; *Hind femora* with dense scale tufts . . . *Lophoscelomyia.*
        - *Thorax* — Narrow-curved and spindle-shaped scales; *Abdomen* — Lateral tufts and small dorsal patches of flat scales . . . . . *Nyssorhynchus.*
        - *Thorax* — Flat spindle-shaped scales
          - *Abdomen* — Nearly completely covered with scales irregularly disposed on dorsum
            - With dense lateral tufts . . *Cellia.*
            - No lateral scale tufts . . *Neocellia.*
          - *Abdomen* — Completely covered with large flat overlapping scales . . *Aldrichia.*
        - *Thorax* — Scales hair-like except a few narrow-curved ones in front; *Abdomen* — Long, broad, irregular scales . . . . . *Kerteszia.*
  - Very small . . . . . *Bironella.*

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Theobald as somewhat indefinite and difficult to interpret; moreover, variations may be met with in the shape and arrangement of the scales—the feature relied on—of any given species. On the other hand, classifications based on the venation of the wings, the structure of the ungues, the shape of the male genitalia or the larval characters, have their disadvantages. Wing venation is often variable; the structure of the ungues has proved of little value; a classification

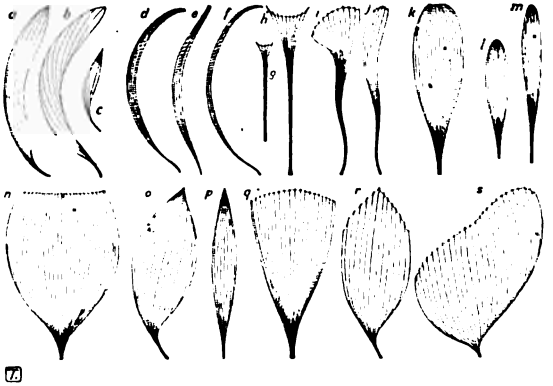

Fig. 37.—Graphic key to generic distinctions based on scale characters.

a, *b*, *c*, Narrow-curved scales; *d*, *e*, *f*, hair-like curved scales; *g*, *h*, upright forked scales; *i*, *j*, long twisted scales; *k*, large lanceolate scale; *l*, *m*, small narrow lanceolate scales; *n*, large inflated scale; *o*, *p*, spindle-shaped scales; *q*, broad flat scale; *r*, *s*, broad irregular scales.

based on larval characters is of no use in the determination of adult specimens. One based on male genitalia is also very unsatisfactory because female specimens are far more abundant and of greater importance. Besides, of some genera we only know the female sex, and years may elapse before we find the corresponding male. A practical classification must necessarily take advantage of various characters, and these must be chiefly adult characters common to both sexes.

Species which have been found to foster the malaria parasites.—Of the large number of described species of Anophelinæ, the following have

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been shown, with more or less precision, to be efficient hosts of the malaria parasites :—

AFRICA.—*Myzomyia funesta, Pyretophorus costalis, Myzorhynchus paludis, M. ziemanni,* Cellia pharoensis.*

EUROPE.—*Anopheles maculipennis, A. bifurcatus, Myzomyia superpicta, Myzorhynchus pseudopictus.*

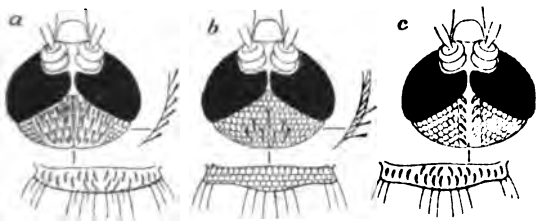

Fig. 38.—Graphic key to generic distinctions based on scale characters.

a, Anopheles, head, scutellum and lateral view of head scales; b, Stegomyia, head scutellum and lateral view of head scales; c, Ædes, head and scutellum scales.

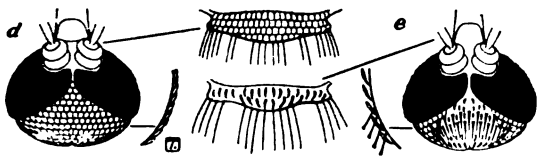

Fig. 38A.

d, Megarhinus, head, scutellum and lateral view of head scales; e, Culex, head scutellum and lateral view of head scales.

NORTH AMERICA.—*Anopheles maculipennis, Cellia argyrotarsis.*

BRAZIL.—*Nyssorhynchus lutzi.*

INDIA.—*Myzomyia rossii, M. culicifucies, M. turkhudi, M. christophersi, Pyretophorus jeyporensis, Myzorhynchus sinensis, M. barbirostris, Nyssorhynchus fuliginosus, N. maculipalpis, N. stephensi, N. theobaldi.*

JAPAN. — *Anopheles formosaensis, A. cohacsus, Myzorhynchus sinensis.*

* Probably a synonym for *M. mauritianus.*

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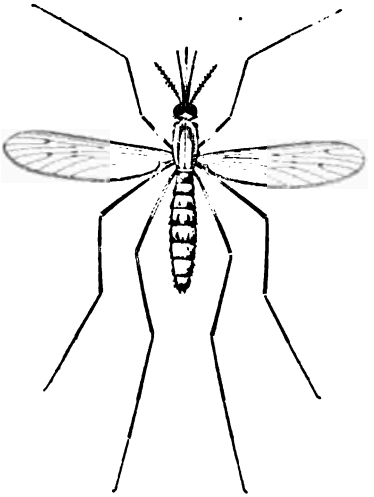

Fig. 39.—Anopheles maculipennis (female).

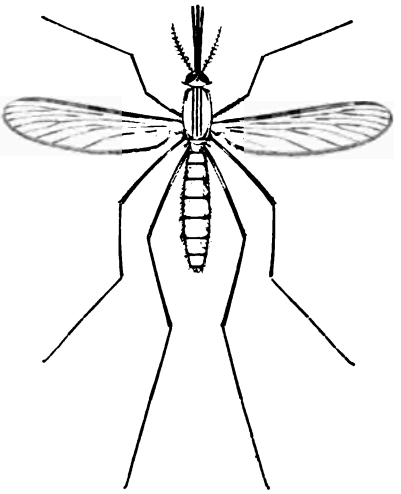

Fig. 40.—Anopheles funestus (female).

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CAMBODIA.—*Anopheles martini, A. pursati.*

TONQUIN.—*Anopheles vincenti.*

MADAGASCAR.—*Myzorhynchus coustani.*

CELEBES.—*Anopheles vagus.*

NEW GUINEA.—*Cellia punctata.*

NEW HEBRIDES.—*Anopheles farauti.*

Fig. 41. — Resting position of Culex pipiens.

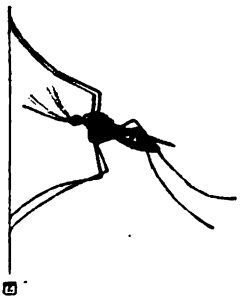

Fig. 42.—Resting position of Myzorhynchus pseudopictus.

Fig. 43. — Resting position of Anopheles maculipennis.

Whether other Anophelinæ are efficient has not been determined. So far no other Culicidæ have been found to foster the malaria parasites of man, and experiments with *Culex albopunctatus*, *C. penicillaris*, *C. vexans*, *C. pulchritarsis*, *C. pipiens*, *Taeniorhynchus richiardii*, *Theobaldinella annulata*, and *T. nemorosa*, have proved negative. Considering that *Culex pipiens* transmits several Hæmoprotozoa of birds, closely allied to those of men, it would be rash to assert positively that the Anophelinæ are the only mosquitoes which transmit the malaria parasite.

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CHAPTER X

TRYPANOSOMIASIS OF MAN

Definition.—Morbid conditions produced by *Trypanosoma gambiense*, including irregular chronic fever, skin eruptions, local œdema, adenitis, physical and mental lethargy.

History.—Although its true ætiology was not apprehended until quite recently, sleeping sickness, the terminal phase of trypanosomiasis, has been known for over a century.

The occurrence of trypanosomes in animals has been recognised for at least sixty years, first in cold-blooded vertebrates, later in mammals. The best-known and first-described mammalian species is that of the rat (*Trypanosoma lewisi*). It was discovered by Lewis in 1879 at Calcutta. In the following year Evans described a similar parasite (*T. evansi*) in the blood of horses in India; he found that it also infests camels, elephants, buffaloes, and dogs, and that it is the cause of the disease called surra which, from time immemorial, the natives of India have ascribed to the bite of certain blood-sucking flies. Fifteen years later Bruce showed that nagana, the fly disease of horses, bovines, and other species of domestic mammals in Africa, is due to the same kind of organism (*T. brucei*). Since these discoveries were made trypanosomes have been found in many species of mammals, as well as in numerous birds, fishes, and reptiles. Though differing in degree of virulence, they all, at least in mammals, give rise to a more or less similar type of disease.*

In 1890 Nepveu, in the course of researches in Algeria on malaria, encountered these flagellates in

* For a brief description of the trypanosomes of mammals the reader is referred to p. 171.

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the blood of man. He appears to have been the first to do so; but, unfortunately, his original description is vague, and his illustrations are crude. He established no definite relationship between the organisms he alluded to and the associated morbid conditions; consequently, his observations did not receive the attention their significance deserved, although, later, he emphatically affirmed that a trypanosome has to be reckoned with as a factor in human tropical pathology.

In 1901 Forde encountered a flagellated parasite in the blood of a European suffering from an irregular non-malarial fever, in the River Gambia Colony. This parasite he showed to Dutton (1902), who recognised it to be a trypanosome. Later, Dutton found a similar organism in the blood of a native of the same colony, and suggested the name *T. gambiense*, which the parasite now bears. Subsequently many cases were described, both in Europeans and natives, and the association of the parasite with a peculiar form of febrile cachexia was quickly and satisfactorily established.

A great impulse was given to the study of the subject by the discovery of trypanosomes in the cerebro-spinal fluid, as well as in the blood of cases of sleeping sickness by Castellani in Uganda in 1902. Castellani's suggestion that the parasite is the cause of sleeping sickness has been fully confirmed by Bruce and other investigators, who have also shown that the tse-tse fly was the probable transmitter of the infection, an hypothesis already advanced on analogical and epidemiological grounds by Sambon and Brumpt.

Geographical distribution. — The presence of *T. gambiense* has been definitely ascertained for the west of Africa from the Senegal in the north to Mossamedes and the upper reaches of the Lualaba in the south. Also in the Congo basin, and in Uganda, where it must have been introduced only recently, apparently about the end of the nineteenth century. Throughout this vast area the infection is not uniformly distributed. It occurs

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in a patchy way, principally along the banks of the rivers and shores of the lakes, conformably to the distribution of certain tse-tse flies, and apparently being influenced also by the frequency and nature of the intercourse and by the occupations of the inhabitants. There is strong reason for believing that the recent influx of Europeans into tropical Africa and the consequent increased movement of the natives is spreading the disease, and that this extension has by no means reached its limit. As regards the eastern side of the continent, the disease has not extended beyond the shores of the Victoria Nyanza. In this locality its present limits are Wadelai on the Nile to the north, and the southern end of Lake Tanganyika to the south. There is

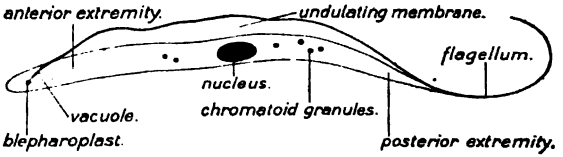

Fig. 44.—Scheme of trypanosoma, with nomenclature.

every reason to apprehend that, in time, the distribution of trypanosomiasis will become coextensive with that of the appropriate tse-tse flies.

Ætiology.—In common with other trypanosomes, *T. gambiense*, as seen in fresh blood, is an active, wriggling organism, having a spindle-shaped body, which is slightly compressed laterally. It is provided with a delicate, wavy membrane—the *undulating membrane*—which fringes the convex dorsal edge of the body, and terminates in a free, whip-like filament, the *flagellum*. Suitably stained specimens show a *nucleus* about the centre of the body, and a minute, deeply staining chromatin mass, the *blepharoplast*, generally near one pole. The extremity of the body which encloses the blepharoplast is regarded by recent authorities as the *anterior extremity;* it varies greatly in shape and may be pointed or obtuse. The opposite end, the *posterior extremity*, tapers to

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a point, to which the flagellum is attached Adjoining or surrounding the blepharoplast is a small non-staining area, the *vacuole*. The free border of the undulating membrane is somewhat thickened; this thickened border springs from the blepharoplast at one end, and its continuation at the other constitutes the flagellum. In certain specimens the cytoplasm is homogeneous; in other specimens comparatively faintly staining granules are visible. In comparing and measuring a large series of specimens, it becomes apparent that there is great diversity in the dimensions of the body of the parasite, the nucleus, and the flagellum.

In certain instances evidences of multiplication by longitudinal division are seen. The process commences most frequently in the blepharoplast, which elongates, and then divides. The nucleus divides almost simultaneously, sometimes before the blepharoplast. The division of the blepharoplast is followed by the duplication of the thickened margin of the undulating membrane, beginning at its blepharoplast attachment; this, in its turn, is followed by longitudinal division of the whole body. The flagellum does not divide; it remains as the flagellum of one of the halves, a new flagellum developing on the other. The fission of the body is effected dorso-ventrally, but the resulting forms do not separate along the ventral border until the new flagellum has appeared, the final separation proceeding postero-anteriorly; parasites still adhering by their anterior extremities are occasionally encountered. The division forms are usually of about equal size, and slightly smaller than the parent form.

Under conditions as yet undetermined, the parasites, which as a rule present a fairly uniform appearance, show a certain variation as regards size, shape, length of flagellum, size of nucleus, and staining reaction of cytoplasm; suggesting indications of sexual differentiation analogous to those exhibited by the gametocytes of the malaria parasites and of other hæmoprotozoa.

Although we are accustomed to observe the parasites in the blood, there is reason to believe that this is not their only or even principal habitat. As suggested by Mott, and proved by Greig and others, they are generally more easily found in the lymphatic glands, which are often markedly enlarged. They occur also in the cerebro-spinal fluid, and probably in the fluid of the serous cavities; facts pointing to the lymphatic system as perhaps the most important habi-

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tat of the trypanosoma. As regards the blood, there is no uniformity in the number of parasites present; sometimes they are fairly abundant here, one or two, perhaps, in each field of the microscope; at other times and in the same patient it may be difficult or impossible, even after prolonged search, to find a single specimen. On the whole, although this is by no means invariable, the parasites are most abundant in the blood during the febrile attacks to which these patients are so subject.

Many attempts have been made to cultivate *T. gambiense* on artificial media, but hitherto without success, notwithstanding that the parasite is readily communicated to monkeys, dogs, rats, guinea-pigs, and other animals, and that in the case of corresponding parasites in lower animals extra-corporeal cultivation has succeeded.

Novy and McNeal have shown that *T. lewisi* and other trypanosomes multiply rapidly in the water of condensation in blood-agar tubes, when suitably cultivated; and that in many species subcultures can be carried on through an indefinite number of generations. In such cultures, however, the trypanosome form may be lost, the flagellum springing directly from the anterior extremity and no undulating membrane developing.

Interesting observations have been made by Laveran and others on a very striking phenomenon exhibited by trypanosomes, under certain circumstances, both in the blood and in artificial cultures. Upon the advent of unfavourable biological conditions in these media, such as the influx of sera of non-susceptible animals, increasing scarcity of nutriment (as in the alimentary tube of an appropriate invertebrate host), lowering of temperature, or the addition of chemical solutions to artificial cultures, the trypanosomes tend to congregate in bunches in which the anterior extremities of the parasites are apposed, the flagellated extremities remaining free. One such group is termed a primary agglomeration, and may be composed of upwards of a hundred individuals. In many cases these primary

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clusters themselves become grouped together to form still larger tangled masses known as secondary agglomerations. Agglomeration does not of itself seem to have any ill effect on the constituent parasites, which may again disperse, apparently quite unaltered. Sometimes all the individuals forming a cluster become disagglomerated; at other times the break up is only partial, a certain number of the more feeble and less mobile parasites remaining together and slowly dying. The significance of this phenomenon has yet to be ascertained. Some authors believe that it indicates a recuperative molecular interchange between the associates.

In cultures, the trypanosomes acquire in many instances a spherical form and undergo multiple division. They lose their flagella in the process, certain of the division forms subsequently acquiring such an organ, which now invariably springs, as already mentioned, directly from the blepharoplast. These culture forms possibly represent a stage in the life of the parasite which, in normal conditions, is passed in the vertebrate host, or more probably in the insect host.

How long a trypanosome infection may persist in the human body has not been definitely determined, but there is evidence that it may continue for at least two years. I have at present (1907) a patient under observation whose infection certainly dates back for that space of time. From what we know of the incubation period of sleeping sickness it is not improbable that this period is sometimes greatly exceeded, and may extend to seven years or longer.

An important practical point is the question of the transmission of the parasite. As already mentioned, the well- and long-known *rôle* of the tse-tse fly* in the transmission of the trypanosome of nagana suggests that the corresponding parasite of man is transmitted by a corresponding insect, a suggestion borne out by considerations of distribution, and, to a certain extent, by experiment.

Minchin, Gray, and Tulloch have shown that when *Glossina palpalis* was half fed on a rat infected

* For a brief description of the tse-tse flies see page 174.

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with the cattle-trypanosome of Uganda (probably *T. brucei*), and immediately transferred to complete its meal on a healthy rat, in four out of five experiments the healthy rat contracted the infection; but if the transference was delayed for an hour even, the experiment failed. As similar experiments with other blood-sucking flies (*Stomoxys*, for example), which, apparently, have no biological connection with *T. brucei*, succeeded to some extent, and as such a method of feeding can only occur exceptionally in nature, it is reasonable to infer that the closely allied *T. gambiense* is not usually communicated in this purely mechanical way. We know that the malaria parasite can be communicated by the direct inoculation of malarial blood, but it is universally admitted that direct inoculation is not the normal method of its transmission. The idea that the glossina inoculated trypanosomes in this direct way originated, undoubtedly, with the interpretation that has been placed on Bruce's experiments with nagana, an interpretation which may be incorrect. It is true that both Bruce and Minchin communicated trypanosoma infection to monkeys and other animals by means of tse-tse flies caught in the jungle. It is manifest, however, that before these tse-tse flies could have fed on the experimental animals an interval of many hours must have elapsed since their previous blood feed. Therefore, in view of Minchin's failure to communicate the disease by insects that had been kept for only a short time after being fed on trypanosoma-infected animals, it is reasonable to conclude that there could have been no direct inoculation by these jungle-caught flies.

A more probable interpretation of the experiments, and one based upon what we know of the transmission of other hæmoprotozoa, is to the effect that glossina serves as an alternative host in a truly biological sense, and not as a simple mechanical transmitter; that the trypanosome, after entering the intestinal canal of the insect, undergoes developmental changes requiring a considerable space

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of time for their completion, developmental changes which enable it subsequently, when the opportunity occurs, to effect a lodgment in the human or other vertebrate host. That this view of the *rôle* of the tse-tse fly is correct, has been practically established lately by Kleine, who, after feeding *G. palpalis* on animals infected with *T. brucei*, set the same flies to bite fresh animals at various intervals. Up to twenty (possibly sixteen) days the flies failed to convey the infection, but from that period onwards to the forty-seventh day, when the experiment concluded, they communicated the trypanosome to eight animals. Bruce has confirmed Kleine's results and has ascertained that they apply to *T. gambiense* and another trypanosome of the dimorphon type.

The trypanosoma-infected contents of the stomach of a glossina if injected into a susceptible animal do not communicate the infection, although the parasites may be alive at the time of the injection. Not improbably the multiplying forms in the stomach are of the same sexual nature as those of malaria in the mosquito—gamete forms—and therefore incapable of multiplication in a vertebrate host. Koch for *T. brucei*, and Minchin, Gray and Tulloch for *T. gambiense*, positively state that the parasites show marked sexual differentiation within the stomach of the insect host. Considering the bionomics of glossina it seems not improbable that some of the trypanosomes, after undergoing certain unknown changes, may enter the larva, and be thus transmitted by heredity to the vertebrate host. This explanation has been suggested by Sambon, and conforms in a remarkable manner to the habits of the babesiæ, and of the leucocytozoa, in relation to their respective invertebrate transmitters.

The discovery by some of the above-mentioned investigators that jungle-caught tse-tse flies harbour a variety of species of trypanosome "wild forms," while only a small proportion of them convey *T. gambiense* (sometimes as many as a thousand of these insects were required before a successful infection of monkeys was effected), makes it evident that

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extreme precision and care must be observed in such experiments in order to eliminate complicating conditions and sources of fallacy. That the tse-tse fly conveys the trypanosome appears to be practically certain, and Koch's observation that trypanosoma forms may sometimes be observed in the blood-free droplet of clear fluid which can be expressed from the proboscis would seem to indicate that the infection is conveyed by the bite of the fly. But, even assuming that glossina has been proved to be the proper transmitter of *T. gambiense*, much still remains to be done: the whole of the history of the trypanosome, from the time of its removal from one vertebrate by the glossina to its introduction into another vertebrate, has to be discovered.

Minchin, having discovered encysted developmental forms of trypanosomes in the lower gut of the tse-tse fly, has recently conjectured that the infection may be transmitted by the droppings of the fly when swallowed by man or other vertebrates.

To settle these and other questions of great practical importance in connection with the *rôle* of the tse-tse fly in trypanosomiasis, experiments with laboratory-reared insects are indispensable; and, further, that observations should be extended to all the species of the genus. We have no assurance that *Glossina palpalis* is the only efficient transmitter.

Predisposing causes.—Neither age, sex, occupation nor race *per se* has any influence on the susceptibility to trypanosoma infection, except in so far as they conduce to the opportunity of infection. Thus occupations (boatmen, fishermen, water-carriers) which imply a frequenting of the water-side haunts of the glossina conduce to infection.

Incubation period.—From Bruce's experiments with *T. brucei* and *T. gambiense*, the incubation period of the glossina-conveyed disease and that of the direct artificial inoculation seem to be about the same, from two to three weeks in the case of dogs, horses and monkeys. As regards man, observations are too few to warrant anything like a definite statement on the point, but in one or two instances circumstances seem to point to a similar incubation period.

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Symptoms.—Without being too definite on the point, and basing the statement on the experience of a limited number of cases, I would suggest that the bite of an infected glossina is followed, in a proportion of cases, by a degree of local irritation of greater or less severity. This subsides in the course of a few days, to be followed, sooner or later, by fever which may last a week or longer, and which may be accompanied by the appearance, in Europeans at all events, of a peculiar type of erythema and a certain amount of serous infiltration of the connective tissue. A form of hyperæsthesia, known as "Kerandel's symptom," is usual; if the patient strikes a limb against any hard object, a degree of discomfort amounting to actual pain is experienced, the sensation being slightly delayed. In time the fever subsides more or less completely, to recur at irregular intervals of days or weeks. The fever is sometimes mild, sometimes severe, occasionally hyperpyrexial (106·6 F.), the evening temperature being always the higher. The fever may last for weeks; the apyretic period may be equally prolonged. On the other hand, the fever may be continuous, or the apyretic period may last for months. Irregularity of degree and duration is a feature of the fever and, also, of the other clinical manifestations of trypanosomiasis. In time the patients become debilitated, anæmic, feeble both intellectually and physically. Headache is very often complained of. The heart's action is generally rapid and easily excited. The cervical glands and the glands of other parts of the body enlarge and may become tender. It may be that only one gland is visibly involved, or there may be a recognisable general polyadenitis, including the abdominal glands. The implicated glands may be very prominent, or they may not be easily felt. Sometimes they are painless, sometimes distinctly painful and tender, rarely suppurating. This condition of irregular fever, of debility, of polyadenitis, of slight anæmia, may go on for months, or even in some instances for years.

There is reason to hope that in a proportion of cases

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the disease may terminate at this stage. I know and have seen three cases in which after many months of illness the symptoms entirely disappeared, and have been absent for several years, during which the parasite could no longer be found in the blood, whether tested by microscope or animal injection (two cases). But, considering that the disease may present at various stages periods of improvement, which in some instances may be very prolonged, it would be rash to say whether in any instance of apparent recovery we are dealing with a radical cure, or merely with one of these long periods of latency. Experiments and observations by Laveran and others in other forms of trypanosoma infection justify the belief that occasionally the parasite does die out, either spontaneously or as a result of treatment.

Remarkable features of human as well as of animal trypanosomiasis are the skin affections and the local œdemas. In many of the lower animals affected with their special trypanosomes, in addition to fever and physical lethargy, papular and pustular eruptions are not uncommon, and in man, especially in negroes, an exceedingly itchy papular eruption is a common symptom. In the European, and possibly in the negro, but in the latter in consequence of his colour not so evident, extensive skin areas are affected with a fugitive, patchy, frequently annular erythema, usually most evident on the chest and back, but also very often on the face and elsewhere. This erythema seems to occur most frequently and most distinctly in the earlier stages of the infection. Some of the patches may extend to six inches or even to a foot in diameter, their margins fading off insensibly into the surrounding normal skin. Sometimes the erythema takes the form of large rings, occasionally complete, more frequently interrupted and irregular. Pressure or any irritation of the skin give rise at once to congestion from vasomotor paralysis of the skin capillaries.

In some of the lower animals a usual feature is œdema of certain parts of the body, especially the sheath of the penis, the under surface of the abdomen,

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and the neck. Similar though less extensive œdemas occur in man, in whom they are most apparent about the face and about the site of the erythema. In many instances there is a general fulness of the features, which, together with concomitant flushing of the face, is apt to convey a false impression of sound health.

Neuralgic pains of different kinds are not uncommon. In one of my cases recurring orchitis, accompanied by an increase of parasites in the blood, was a feature. Painful local inflammatory swellings, which after a time subside without suppuration, I have seen in three cases.

In most cases the spleen is enlarged, sometimes enormously enlarged, the swelling fluctuating with the fever. The liver also may be enlarged. As the patients affected with trypanosomiasis are usually the subjects of malarial disease, it is not always possible to say whether the enlargement is entirely or partly attributable to the trypanosome.

Sleeping Sickness.—The condition known as sleeping sickness may be regarded as the terminal stage of trypanosoma infection. Sometimes it exhibits acute features, sometimes it is exceedingly chronic. From the commencement of the infection to the development of this terminal stage in a proportion of instances an interval of many years, possibly seven, may elapse In the majority of cases the march of events is much more rapid. The characteristic symptoms depend on implication of the nervous system, either by the parasite itself or by its toxines.

According to Low and Castellani, the average duration of this stage of trypanosomiasis is from four to eight months, not infrequently less; very chronic cases with a course of more than a year's duration are rare. Other observers refer to cases running on for three years, or even longer, and presenting occasionally temporary ameliorations.

Generally the first indications of the oncoming of sleeping sickness are merely an accentuation of the debility and languor usually associated with trypanosoma infection. There is a disinclination to exertion; a slow, shuffling gait; a morose, vacant

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expression; a relaxation of features; a hanging of the lower lip; a puffiness and drooping of the eyelids; a tendency to lapse into sleep or a condition simulating sleep; a slowness in answering questions; a shirking of the day's task. Dull headache is generally present. Later there may occur fibrillary twitching of muscles, especially of the tongue, and tremor of the hands, more rarely of the legs, indicating a definite implication of the motor centres. By this time the patient has taken to bed, or he lies about in a corner of his hut, indifferent to everything going on around him, but still able to speak and take food if brought to him. He never spontaneously engages in conversation or even asks for food. As torpor deepens he forgets even to chew his food, falling asleep perhaps in the act of conveying it to his mouth, or with the half-masticated bolus still in his cheek. Nevertheless, such food as he can be got to take is digested and assimilated. Consequently, if he is properly nursed, at this stage there may be no general wasting. As time goes on he begins to lose flesh, tremor of hands and tongue becomes more marked, and convulsive or choreic movements may occur in the limbs or in limited muscular areas. Sometimes these convulsions are followed by local temporary paralysis. Sometimes there is rigidity of the cervical muscles and retraction of the head. Bedsores tend to form, the lips become swollen, the saliva dribbles from the mouth; gradually the lethargy deepens, the body wastes, the bedsores extend, the sphincters relax, and finally the patient dies comatose or sinks from slowly advancing asthenia. Possibly he succumbs to convulsions, hyperpyrexia, pneumonia, dysentery, or other intercurrent condition.

The manifestations described are subject to considerable variations. Mania is not uncommon; delusions may present themselves, or psychical and physical symptoms not unlike those of the general paralysis of the insane are developed.

During the whole course of the nervous stage of trypanosomiasis the other symptoms already described as characteristic of the infection may be in evidence.

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The knee jerks, though lost towards the end, are active at first; the fundus oculi is normal; the sphincters, until towards the end, are controlled; the urine is normal, and the bowels, although generally tending to constipation, act with more or less regularity.

Mortality.—Although spontaneous recovery may take place in the early stages of trypanosomiasis, when the disease has arrived at the stage of sleeping sickness death is believed to be inevitable. Corre has told us how native villages in Senegambia have been depopulated. What has occurred on the Congo, in Angola, and recently in Uganda, bears out this estimate of the gravity of the disease when it appears in epidemic form. We know that many islands on the Victoria Nyanza have been completely depopulated, and if it be true for a large part of the country, as Bruce has shown to be the case at Entebbe and its neighbourhood, namely, that 30 per cent. of the population harbour trypanosomes, the outlook for Uganda and neighbouring countries is grave indeed. The population of the implicated districts of Uganda, originally about 300,000, has been reduced in six years to 100,000 by sleeping sickness.

Morbid anatomy.—No gross lesions of the nervous centres, or of any other organ, have been described as being invariably present; but in every case indications, principally microscopical, of an extensive meningo-encephalitis can be demonstrated. In a proportion of instances congestion of the meninges, effusion of lymph, increase and turbidity of cerebral fluid, are found. In all cases, as first pointed out by Mott, there is an extensive small-cell infiltration of the perivascular lymphatic tissue throughout the brain, cord, and meninges, varying in amount in different cases and in different anatomical regions. This, the essential pathological feature of sleeping sickness, recalls the very similar condition in the general paralysis of the insane.

The nervous elements exhibit secondary degeneration changes.

Similar changes are described by Mott in the nervous system in dourine, and chronic trypanoso-

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miasis in the monkey. Mott has also pointed out that the lymphatic tissues throughout the body are similarly affected.

Bettencourt and other Portuguese observers, as well as Castellani, have described a diplococcus in the brain in sleeping sickness. This organism is in no sense causally related to the disease; it must be regarded merely as a terminal and non-essential epiphenomenon. Similarly, *Filaria perstans* (which at one time, in consequence of considerations of fre-

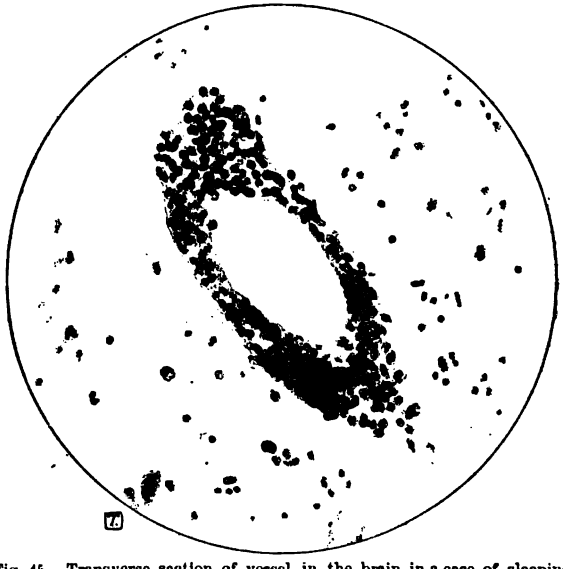

Fig. 45.—Transverse section of vessel in the brain in a case of sleeping sickness. (*From photo after Bettencourt.*)

quency of concurrence and geographical distribution, was regarded as being possibly the cause of the disease), the various intestinal worms and *Schistosomum hæmatobium*, though often met with in sleeping sickness, are present only as accidental concurrences.

Diagnosis.—Diseases with which trypanosomiasis might be confounded are kala-azar and pellagra and, in its later stages, beriberi.

As regards beriberi, there should be no difficulty if it be borne in mind that it is a disease of the peripheral, whilst trypanosomiasis is a disease of the

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central nervous system; that beriberi is non-febrile, and that trypanosomiasis is febrile. Kala-azar and trypanosomiasis, especially in their earlier stages, may be more difficult to differentiate; but the presence of enlarged glands, local œdema, and erythema multiforme in trypanosomiasis, and their absence in kala-azar, suffice for distinction. Blood or gland-lymph examination, or, if this be negative, hepatic or splenic puncture, should establish the diagnosis.

In pellagra the erythema is of a characteristic type. It is not ringed or fugitive as that of trypanosomiasis, and it affects principally the exposed parts of the body; the disease is of a much more chronic character, and, instead of lethargy, the mental condition is more that of insanity—melancholia alternating with mania and terminating in dementia. Further, in pellagra, the symptoms are aggravated at particular seasons—spring and autumn.

The microscopical diagnosis of trypanosomiasis is sometimes difficult. Anæmia as well as a large mononuclear leucocytosis occurs in trypanosomiasis. A wet blood preparation exhibits, even to the naked eye, a remarkable clumping of the red corpuscles. Held up to the light, such a preparation has a peculiar granular appearance produced, as can be seen on microscopical examination, by agglomeration of the corpuscles into heaps and clusters, the usual rouleaux arrangement being absent. Such a disposition of corpuscles is significant of trypanosoma infection. As a rule, the parasites in the peripheral circulation are few in number, many fields having to be hunted before a single example is discovered. Sometimes none can be found; rarely are they abundant. In the same case they are sometimes present, sometimes absent. Centrifuging the blood is not of much assistance. Dutton and Todd have called attention to the value of lymphatic gland puncture and examination of the aspirated lymph. An ordinary hypodermic syringe suffices to aspirate a sufficiency of lymph. Films of the lymph so obtained are prepared and stained in the ordinary way.

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Cerebro-spinal fluid, obtained by lumbar puncture and centrifuged, affords another, though not always a practicable means of finding the parasite.

The trypanosome is easily stained by most dyes; convenient stains are those in use for malaria work. A sixth objective suffices to find the parasite.

Treatment.—So far, we have no assurance that *T. gambiense* can be eradicated by any ordinary and safe therapeutic measure. Like other trypanosomes, it is undoubtedly to some extent amenable to large doses of arsenic, more especially if given in combination with certain aniline colours. By such means trypanosoma infections have been eradicated in the rat and mouse, and undoubtedly encouraging results have been obtained by similar measures in man. Good results have accrued from alternating doses of trypanroth and arsenic; but as trypanroth, if persisted in, is apt to give rise to nephritis, its use over long periods is not advisable. A safer and more potent form of arsenic has been introduced by Thomas, namely atoxyl, a meta-arsenic-anilin compound. I have given this drug in six cases—Europeans—with most encouraging results, and Koch, Broden, Campenhout, and others speak most hopefully of its value. It is best given intramuscularly in 10 or 20 per cent. solution in distilled water, commencing with one grain every third day, increasing the dose to three grains. Others give the drug in much larger doses, up to 10 grains, more or less frequently repeated. These large doses, I hold, are unnecessary and, as in a considerable number of cases they have caused blindness, must be used with caution. As soon as toxic symptoms—generally pain in the abdomen—show themselves, the dose is lowered a little and kept up for months.

Lately, Thomas has had favourable results in animal trypanosomiasis from mercury, and suggests a trial of the salts of this metal in man.

The effect of the administration of arsenic compounds on a heavily infected animal are very marked, after a preliminary and marked increase in their members in the peripheral circulation. According to

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Thomas, in from three to seven hours an adequate dose of atoxyl causes the trypanosomes to become swollen, deformed, and almost motionless, their cytoplasm taking on a peculiar ground-glass appearance, becoming vacuolated, and presenting large dark granules. After seven or eight hours, coincidently with a marked increase of leucocytes—especially phagocytes—the parasites become rapidly fewer in number, and by the sixteenth or eighteenth hour completely disappear.

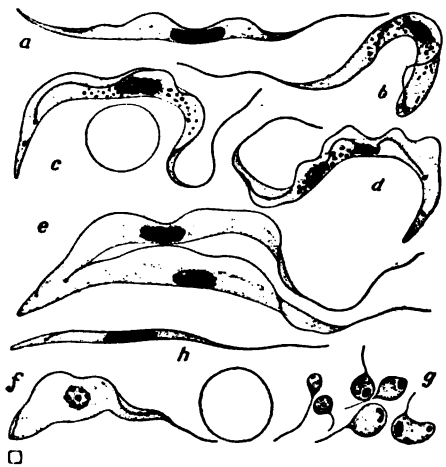

Fig. 46.—Trypanosoma gambiense: various forms from blood and cerebro-spinal fluid.

a, Elongated anterior extremity; *b*, blunt ditto; *c*, *d* and *e*, dividing forms; and *h*, probably sexual forms; *g*, small round forms from cerebro-spinal fluid.

Antimony in the form of sodium tartrate hypodermically has been shown by Plimmer and Thompson to cause, without the production of serious local irritation, almost immediate and often permanent disappearance of the trypanosomes in infected rats. In two cases in man in which I used this drug hypodermically the consequent local pain and irritation were so excessive that in this form the treatment had to be abandoned. One of the patients, however, continued the drug by mouth to the extent of one and a

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half to two grains daily, very highly diluted, and along with atoxyl injections, for over one year. He appears to be quite well. I have heard of similar experiences, and believe that in antimony by the mouth, or intravenously, we have a promising specific.

Soamin, an arsenical compound similar to atoxyl, appears to be equally effective, and may be used in the same way.

In the treatment of trypanosomiasis, concurrently with the use of drugs, every effort should be made to keep the patient in good general health. Rest, warmth, and residence in a cool and healthy climate, the systematic use of quinine for any concurrent malarial infection, and the avoidance of fatigue and everything that might depress, should be insisted on.

The idea of cure must not be entertained until the patient has been free from all symptoms for many months, nor until the repeated injection of several cubic centimetres of his blood has failed to induce trypanosomiasis in susceptible animals.

Immunisation.—Attempts have been made to procure a curative and immunising serum, but, although a certain amount of success has attended these efforts in respect to the lower animals, as regards man they have failed.

Prophylaxis.—The indications for prophylaxis are based principally on the habits of *Glossina palpalis* and the existing conditions as regards the presence of the infection in a locality.

In endemic regions the fly areas should be located and avoided. If such regions have to be traversed the journey should be made during dark nights, when tse-tse flies do not feed, or with such precautions as are used by the natives for the protection of their cattle in nagana-infected spots. Those who are compelled to live in tse-tse regions should have their houses and persons carefully guarded against the fly. Manifestly it is desirable —whether it is feasible is another question — to avoid localities in which the natives are affected, and to prevent the infection of the local tse-tse flies by surrounding people having trypanosomes in their blood

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with mosquito netting; or by other measures, such as removing them from the usually very limited fly area to some neighbouring fly-free spot. Movements of infected individuals towards hitherto uninfected countries must necessarily be attended with great risk of the introduction of the disease. Whether such movements can be prevented in savage lands depends greatly on local circumstances. Wherever possible they should be prevented. Dutton and Todd suggest that an easily ascertained condition, more or less general in trypanosomiasis, namely, enlargement of the cervical glands, should be employed in eliminating dangerous individuals. Many years ago slave-dealers used such a method to shield themselves from loss. As a rough test it has some value. But we know that in some cases of trypanosomiasis the glands are not appreciably enlarged at all times, so that such cases could easily slip through a quarantine station. Moreover, as the cervical glands are often enlarged in other conditions, an injustice might be done in enforcing such a measure in every instance.

Hodges and his colleagues in Uganda inform us that the fly ground proper is always a very narrow strip indeed, not more than ten to fifteen yards, and always along the water's edge; and that the insects very rarely extend their feeding beat beyond sixty yards of this, whether on the land side or on the water side. It is true they may follow with great persistency a man who has just passed through this narrow belt, for several hundred yards, rarely as far as half a mile; but it is obvious that if the ten or fifteen yards at the water's edge be made unsuitable for the fly, as can readily be done by clearing it of jungle, there will soon be no flies to follow, and the place will become safe. Therefore, where feasible, fly spots, where there are landing-places, ferries, wells or roads, should either be avoided altogether or be cleared of jungle for some yards—to be safe, thirty—from the water's edge. This is a practical measure of proved value in Uganda.

Koch, from observations in Uganda, has suggested that trypanosomiasis may be communicated by the

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male during coitus. The phenomena of dourine and recent animal experiments support the idea, although the experiments referred to indicate that the risk is not great.

A complete scientific prophylaxis can be indicated with certainty only when we have full knowledge (1) of the habits of the tse-tse flies and of the reasons for their restriction to very limited and apparently capriciously distributed areas; (2) as to what vertebrates under natural conditions are normally hosts of *T. gambiense*. Experiment has shown that the glossina will bite any vertebrate, and that it can infect a large variety of animals with the trypanosome. If this be the case in the laboratory it is reasonable to suppose that it is the case in nature also. Therefore, in the endemic regions of trypanosomiasis, the vertebrate fauna has to be reckoned with as a source of infection.

The introduction of *T. gambiense* into other countries, is a grave possibility. It is true that it must have been frequently introduced into America in the days of slave importation and that it did not spread there; but as regards India and other Asiatic countries, which hitherto have had no communication with the West Coast of Africa, the experience has not been made and we have no assurance that if introduced the parasite would not find some appropriate transmitter. According to some authorities, nagana and surra are the same disease; if so, the causal trypanosome can be transmitted by blood-sucking flies other than the tse-tse. What holds good for *T. evansi* and *T. brucei* might equally apply to *T. gambiense*.

OTHER FORMS OF TRYPANOSOMIASIS IN MAN.

Seeing that most of the trypanosomes hitherto studied experimentally are capable of living in a variety of vertebrate hosts, it seems probable that other members of this group of parasites, in addition to *T. gambiense*, may find in man at times a suitable host. Apparently *T. lewisi* and *T. brucei* do not thrive in man, but that circumstance does not warrant the inference that he is immune against all other species.

Some three years ago Lacedra stated that he had

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found a trypanosome in the spinal cord of a patient who had died of supposed beriberi in a lunatic asylum in Brazil, and quite recently Chagas describes a trypanosome disease occurring in the state of Minas, Brazil, in which the trypanosome, identified as *T. cruzi*, is transmitted by a bug—*Conorrhinus*.

TRYPANOSOMES OF MAMMALS.

Of the trypanosomes of mammals the best known and most important are the following:—

T. lewisi (Kent, 1879) is a parasite of rats (*Mus decumanus*, *M. rattus*, *M. rufescens*). Similar parasites in hamsters, guinea-pigs, rabbits, etc., probably belong to different species; *T. lewisi* is not capable of living in these animals.

On account of the facility with which it can be procured in most countries, *T. lewisi* offers the best opportunity for study of the genus. In many places from 2 to 50 per cent. of the local rats harbour it, often in such abundance that, viewed

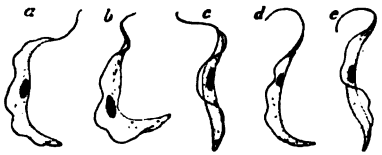

Fig. 47.—Trypanosomes, × 1000.
a, T. equinum; *b*, T. brucei; *c*, T. equiperdum; *d*, T. lewisi; *e*, T. evansi.

through the microscope, the blood seems to seethe and quiver with the rapidly moving parasites. Specimens are easily procured by snipping off with scissors the tip of the rat's tail and dabbing the cut surface on the slip.

T. lewisi measures on an average, including the flagellum, 24-25 μ by 1·5 μ; the anterior extremity is said to be more pointed than in the other known mammalian trypanosomes. The nucleus is situated in the posterior half or third of the body; the cytoplasm is very clear and free from granules. There is evidence that it is conveyed from rat to rat by *Hæmatopinus spinulosus*, the rat-louse, which, according to the researches of Prowazek, is a true alternative host. Probably the rat-fleas also may serve as transmitters.

It is generally held that *T. lewisi* is non-pathogenic. Certainly rats usually exhibit a remarkable tolerance towards this parasite, but occasionally they do sicken and die.

The fact that the rat is susceptible to laboratory inoculation with the trypanosomes of man and cattle indicates the possibility of finding other species of trypanosomes in the blood of wild rats.

T. evansi (Steel, 1885); length, 22-30 μ; breadth, 1-2·5 μ. This parasite was discovered in 1880 by Griffith Evans in the

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Punjab, in the blood of horses suffering from surra, a disease which the natives of India ascribe to the bite of certain horse-flies (*Tabanidæ*). *T. evansi* is not limited to horses and mules, but attacks also camels, elephants, buffaloes, and dogs. Experimentally it has been transferred to monkeys, rabbits, rats, mice and guinea-pigs. It has a very wide distribution in Southern Asia and in Malaya. It has been recently imported into Mauritius and the Philippines. We have no positive knowledge as to the definitive host or hosts of this trypanosome. Various blood-sucking flies belonging to the genera *Stomoxys*, *Hæmatobia*, and *Tabanus* have been incriminated. In Mauritius the epidemic is thought to have been spread by *Stomoxys nigra*.

The disease known as "Mbori," occurring among dromedaries coming from the Sahara into the Soudan (Timbuctoo, etc.), which is apparently also conveyed by a tabanus, is considered both by Vallée and Panisset, and Laveran and Mesnil to be a milder form of surra, the parasite which causes it being a "variety" of *T. evansi*.

T. brucei (Plimmer and Bradford, 1899); length, 28-30 μ; breadth, 1·5-2·5 μ. The anterior extremity is usually bluntly rounded. The cytoplasm often contains in the posterior half large, deeply staining granules. This parasite was discovered by Bruce in 1895 in the blood of horses suffering from nagana, the fly disease of Africa. The normal intermediary hosts of *T. brucei* are probably some of the African *Antilopidæ*, such as the wildebeest (*Catoblepas gnu*), the koodoo (*Strepsiceros capensis*), and the bushbuck (*Tragelaphus scriptus sylvaticus*), perhaps also buffaloes. Bruce's researches and experiments led to the belief that the disease was transmitted in a mechanical way by *Glossina morsitans*. Mr. Austen has shown that the tse-tse flies with which Bruce made his experiments belonged chiefly, if not entirely, to the species *G. pallidipes*, and now we know that other glossinæ, such as *G. fusca*, may also convey the disease, and that the *rôle* played by these flies is probably that of true alternative host.

With the exception of man, and, perhaps, of certain strains of donkey and goat, all domesticated mammals hitherto experimented with, on inoculation with blood containing the parasite, acquire nagana.

After inoculation of an animal with nagana blood, in from one to two days trypanosomes begin to appear in the blood, and persist therein till death, which, in the vast majority of species, is inevitable. In some species (rats, mice) the trypanosomes become very numerous; in others (the rabbit, guinea-pig) they are scanty and may be hard to find with the microscope, although their presence may readily be proved by the symptoms and by injection of the suspected blood into the rat. After inoculation death occurs in rats and mice in from two to three days, in rabbits in from five to twelve days, in guinea-pigs in about fifty days (extremes 20 to 183 days), in dogs in from twenty-two to twenty-six days, in monkeys in fifteen days, in horses and donkeys in from one week to three

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months, in goats and sheep in several months, and in cattle in from one week to six months, a proportion recovering. Thus resistance varies within wide limits both as regards the individual and also as regards the species.

In those animals in which death occurs within a few days of infection the parasites become very numerous, and, after one or two oscillations of temperature, death occurs suddenly. In those animals in which death is delayed a very striking cachexia is established. There is a chronic recurring fever, the numbers of parasites visible in the blood being greatest during the febrile accessions; there is also a peculiar firm œdema from infiltration of coagulable lymph into the connective tissue of the neck, abdomen, sheath of penis, genitals, and limbs; intense anæmia, wasting, skin eruptions, and, often, blindness. On *post-mortem* examination the spleen is in most instances found to be enlarged, ecchymoses may be present in various viscera, and the lymphatic glands corresponding to the point of inoculation are swollen.

Other trypanosomes, more or less allied to *T. brucei*, and possibly representing only varieties of the same parasite, have been observed in German East Africa and Togoland among cattle, horses, and other animals. Again, the disease known as "aino," which occurs in Somaliland among dromedaries, and which Brumpt believes to be transmitted by *G. longipennis*, locally termed the "aino," is probably a variety of nagana.

T. equiperdum (*T. rougeti*), Dofl., 1901—length, 25-28 μ; breadth, 1½-2 μ—differs from *T. brucei* in not having prominent granules in the cytoplasm. It is the cause of a peculiar disease in stallions, brood mares, and donkeys, occurring in South Europe, North Africa, Chili, and probably in the United States, and known as dourine or mal du coït. The latter name it has received from the fact that, as a rule, the infection is communicated through coitus. It is not yet certain whether the parasites have any alternate insect host into which they must pass at intervals in order to complete the life-cycle. Fleas have been suggested as possible intermediaries.

Symptoms appear in from ten to twenty days after infection. They begin in the case of the stallion with œdema of the sheath and some inflammation of the end of the penis and discharge from the urethra; in the mare there is a similar œdema of one or both labia and a muco-purulent vaginitis. Concurrently with increase of these symptoms, œdema of the limbs and of the abdominal walls sets in, together with progressive anæmia, wasting, muscular weakness, flexion of the fetlocks, and skin eruptions. The appetite is preserved. Fever, except at the outset (40° C.), rarely exceeds 39° C. The disease continues for many months—four to ten. Before death weakness increases, the cornea may ulcerate, and there may be complete paraplegia from softening of the spinal cord.

The trypanosome of dourine occurs in the blood, but in numbers so scanty that to communicate the infection with certainty by this medium it may be necessary to inject from

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10 to 15 c.c. Hence the improbability of infection by biting insects. On the other hand, it occurs in great abundance in the œdematous tissues, in the skin lesions, and in the discharge from the genitals.

In marked contrast with *T. brucei*, *T. equiperdum* is but feebly pathogenic to rats and mice, some of the former being quite refractory. In the rabbit and dog the disease resembles that in the horse, and is communicable by coïtus. Monkeys, goats, sheep, and bovines are said to be insusceptible.

Although in many respects the parasites of dourine and nagana resemble each other, the differences in susceptibility of various animals as regards the two parasites indicate specific difference.

T. equinum (Voges, 1902); length, 22-55 μ; breadth, 1·5-2 μ. This parasite is clearly distinguished from the above-mentioned species by the very minute size of its blepharoplast. The cytoplasm contains granules, but not so numerous as in *T. brucei*. Its normal vertebrate host is probably the Capybara, *Hydrochærus capybara*, a large water mammal of South America belonging to the family *Caviidæ*. Nothing positive is known about its transmitting agent; *Stomoxys calcitrans* and *Stomoxys nebulosa* have been blamed. *T. equinum* causes in horses a deadly disease known as mal de caderas in Brazil, Argentina, and Central South America.

T. theileri.—Laveran (1902) reports the discovery by Theiler in the Transvaal of a trypanosome twice the size of any of the foregoing, and peculiar to cattle; so far, other domestic animals have been found to be immune. Theiler regards the disease it produces as an acute pernicious anæmia without poikilocytosis, and with only slight accompanying fever. He considers "that there exists a natural immunity in cattle against this trypanosome." Theiler believes that the transmitter of this parasite is a spider-fly, *Hippobosca rufipes*. Another species, *H. maculata*, recently imported with cavalry from India, is believed to be aiding in spreading the disease. The disease is known as *galziekte*, or bile-sickness, in the Transvaal.

THE TSE-TSE FLIES (Plate III.).

(Genus *Glossina*, Wiedemann, 1830.)

The *Glossinæ* are sombre-coloured, narrow-bodied flies from about 8 to 12 mm. long, with a thick proboscis (*i.e.* proboscis enclosed by the palpi) projecting horizontally in front of the head. Their wings are large, of a brownish hue, and present a characteristic venation (Plate III.) somewhat resembling that of the warble-fly (*Hypoderma*). The most striking peculiarity in the wing is the course of the fourth longitudinal vein, which about the middle of the wing bends abruptly upwards to meet the short and very oblique anterior transverse vein; here, describing a right angle, it runs obliquely downwards to meet the posterior transverse vein, and then turns upwards to reach the margin of the wing near the apex. When the tse-tse is at rest its wings overlap on the back, crossing each other like the

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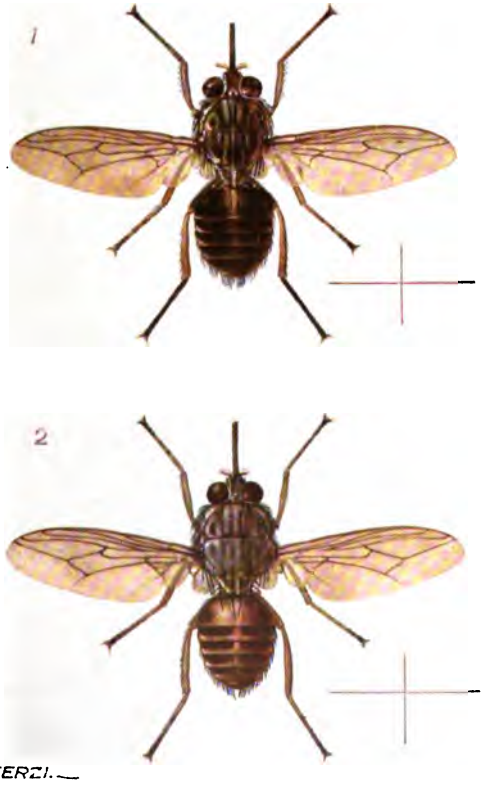

PLATE III.—Tsé-tsé Flies.
1, Glossina palpalis; 2 G morsitans.

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blades of a pair of scissors (Fig. 48 and Plate III.). This resting attitude of the wings, besides giving the fly a peculiar elongated appearance, renders it readily distinguishable from those other blood-sucking diptera with which it might be confounded, such as the stinging-fly (*Stomoxys*) and the cleg (*Hæmatopota*). *Stomoxys* is smaller in size, has a slender proboscis, and its wings diverge at an angle when resting. *Hæmatopota* presents long, prominent antennæ and its wings are tectiform, *i.e.* they meet together at the base like the roof of a house and diverge slightly at the tips. In some species the abdomen is crossed by sharply defined dark brown stripes, interrupted at the middle line. In the males, beneath the end of the abdomen, the external genitalia form a conspicuous knob-like protuberance, which renders the sexes easily distinguishable.

The palpi are long, deeply grooved on their inner sides and closely applied to the proboscis, which they almost entirely conceal, the only uncovered portion being a peculiar large bulb-like expansion at the base. The proboscis consists of three parts (Fig. 48A), *labrum*, *hypopharynx*, and *labium*.

The genus *Glossina* belongs to the sub-family MUSCINÆ, of the family MUSCIDÆ. The nearest related genera are *Stomoxys*, *Lyperiosa*, *Hæmatobia*, *Beccarimyia*; but on account of its limitation to Africa, its peculiar structural features (bulb at the basis of proboscis, remarkable male genitalia, characteristic venation of wings), and its aberrant mode of reproduction, it presents a marked individuality.

The genus comprises **ten species**, which may be distinguished as follows:—

- GENUS GLOSSINA.
  - Large species; length of body at least 11mm.
    - Thorax with four sharply defined dark-brown oval spots . . . *G. longipennis.*
    - Thorax without spots . . . . . *G. fusca.*
  - Small species; length of body rarely reaching 11mm.
    - Hind tarsi black
      - Antennæ black
        - Two last joints of front tarsi black
          - Abdomen not very marked — *G. palpalis.*
          - Abdomen conspicuously marked — *G. tachinoides.*
        - All joints of front tarsi yellow . . . *G. bocagei.*
      - Antennæ yellow . . . . . *G. palliceva.*
    - Two last joints of hind tarsi black
      - Front and middle tarsi yellow . . *G. pallidipes.*
      - Front and middle tarsi black
        - Abdominal stripe ½ of segment — *G. morsitans.*
        - Abdominal stripe ⅓ of segment — *G. longipalpis.*

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Distribution.—Tse-tse flies are confined to Africa. Some species, such as *G. fusca* and *G. morsitans*, have a very wide range throughout the greater part of intertropical Africa. *G. palpalis* is also widely distributed, ranging from the Senegal to the Cunene on the west, and throughout the Lualaba-Congo system to the Victoria Nyanza and upper Nile at least as far north as Moolo in the Soudan. *G. longipalpis* is recorded from French Guinea, the Congo, and the Zambesi. *G. pallidipes* is found throughout East Africa. Other species appear to be more restricted. *G. longipennis* is limited to Somaliland and adjacent regions; *G. tachinoides* to Lake Chad; *G. pallicera* to the Ivory Coast. We should not forget, however, that the limits of the various species are very imperfectly known. Far more definite and important is the knowledge of their topographical distribution. The *Glossinæ* are never found on mountains; they are seldom seen above 3,000 feet; they are absent from extensive plains or other open places; they are rarely found in close cultivation. Their habitat is always in the neighbourhood of open water—along the banks of rivers, brooks, and springs, round the coasts of lakes, on low riverine islands, in swamps and mires, with open pools and sandy banks, especially at the foot of mountains. A sudd-covered or sedgy-banked river or lake shore or sedgy swamp they do not frequent. They are most numerous along the water's edge; they become scarcer and scarcer as one advances inland, and disappear entirely within a few miles of the water. The places they occupy are sharply defined and, as a rule, permanently established. These places or stations are called "fly belts," and the natives know the limits of these belts precisely. The fly belts vary greatly in disposition and extent. Not infrequently they occur on one side of a stream, but not on the other. These fly patches are usually confined to strips of jungle, to banana grounds coming down to the water's edge, or to areas of mosani or mimosa forest. In short, the essential condition of a tse-tse station are—the presence of open water, a wooded district, and a loose soil. As a rule, the fly patches are in sandy ridges or where there are overhanging or jungle-shaded banks.

The limitation of the tse-tse to definite tracts or "belts" has given rise to much speculation. The prevalent opinion is that the fly waits near water to feed on the animals that come to drink. Mr. Austen ascribes it to a characteristic social tendency which is exhibited very frequently amongst Diptera. Sambon suggests that it may be related to some food habit—possibly to a connection with air-breathing fish, of which there are several genera (*Clarias*, *Clarialabes*, *Channallabes*) with numerous species in the rivers and lakes of Africa; the fly either feeding directly on the fish or on some mammal or bird which feeds on these fish. Such an association with air-breathing fish might explain the peculiar patchy distribution of tse-tse flies, their limitation to the neighbourhood of water, and the sandy and thickly wooded nature of their haunts. For in the dry season the air-breathing fish are obliged

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to bury themselves in the mud or to excavate burrows from which they come out towards evening in quest of food; they must therefore necessarily congregate in such places as offer conditions suitable to these habits.* It is very important to ascertain the exact reason for the singular topical limitation of the fly, for it may be that through knowledge of this the prophylaxis of fly-transmitted disease could get its opportunity.

Reproduction.—The *Glossinæ* do not lay eggs as do the majority of the Diptera, but, as in the case of forest-flies (*Hippoboscidæ*), the eggs hatch, and the larvæ feed, develop and moult within the body of the parent, so that when extruded they have practically reached the pupa stage. In fact, the extruded larva becomes almost immediately a pupa, the larva skin becoming a dark, rigid puparium. When extruded, the fully grown larva is nearly as large as the abdomen of the mother; it is a yellowish ovoid body composed of twelve segments and presenting two small hooks at the anterior pole, and two protuberances at the posterior extremity, which is black. The perfect insect emerges from its pupa-case in about six weeks. In the case of *G. palpalis* the pupa has been found in Uganda buried in the loose earth about the roots of banana trees (Bagshawe).

Habits.—Tse-tse flies are voracious blood-suckers, exhibiting great persistency in their attacks on man and animals. They bite almost exclusively during the day. Contrary to what is the case among horse-flies (*Tabanidæ*) and mosquitoes (*Culicidæ*), of which the females alone suck blood, in the tse-tse both sexes are blood-sucking.

* It is interesting to note in connection with this suggestion that quite recently trypanosomes of the mammalian type have been found by Dutton, Todd, and Toby in *Clarias angolensis* at Leopoldville, and by Montel in another air-breathing fish of undetermined species.

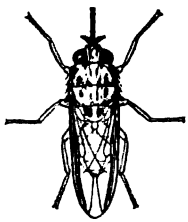

Fig. 48.—Tse-tse fly.

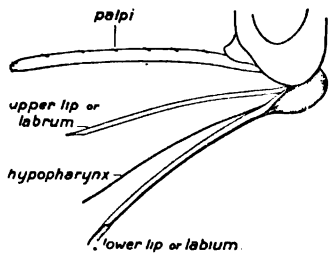

Fig. 48A.—Mouth parts.

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CHAPTER XI

KALA-AZAR

Synonyms.—Tropical splenomegaly, black sickness, Sirkari disease, Sahib's disease, Burdwan fever, kala-dunkh, dum-dum fever.

Definition.—An infective disease characterised by chronicity, irregular fever, enlargement of the spleen and often of the liver, the presence of the "Leishman body" in these and other organs emaciation, anæmia, frequently a peculiar hyperpigmentation of the skin, and a high mortality.

History.—The earliest description of this disease is by Clarke, who states, in the Assam Sanitary Report for 1882, that as far back as 1869 the attention of administrative officers in Assam had been directed to a peculiar disease called by the natives kala-azar, the ravages of which decimated, and in some instances almost depopulated numerous districts in the Garo Hills. Notwithstanding its peculiar clinical features, its great fatality, its mode of spread along the lines of communication, the almost constant absence of malaria parasites from the blood, and the inefficacy of quinine treatment, until quite recently kala-azar was regarded by the majority of physicians as "a bad form of malaria."

In 1889 Giles, who had been appointed to investigate the ætiology of kala-azar, denied its malarial nature, and stated that the disease was "neither more nor less than ankylostomiasis," because he found the ova of the hookworm in the fæces of practically all the cases he investigated. Giles's theory furnished a plausible explanation of the peculiar way in which kala-azar spread, and which could not be satisfactorily accounted for by the malaria theory. It was accepted by some, with the reservation, however, that he had underestimated the malarial element. Dobson strongly

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opposed the ankylostoma theory. He stated that in 116 cases of kala-azar he had found the hookworm in 75 per cent., in 212 cases of other illness he had found it in 73·20 per cent., and in 146 healthy men he had found it in 67·12 per cent.

In 1896 Leonard Rogers and in 1898 Ronald Ross were appointed to re-investigate the disease. Both agreed as to its malarial nature; the former regarding it as a malignant type of malaria, the latter as malarial disease to which some form of secondary infection was superadded.

In 1903 Bentley endeavoured to prove that kala-azar was a malignant form of Mediterranean fever, a disease which he suggested was probably introduced into India at the time of the Mutiny by British troops from Malta, Gibraltar, and other Mediterranean ports.

Owing to the absence of malaria parasites in the cases of tropical splenomegaly I had studied in this country, the absence of tertian and quartan periodicity in the fever, and the uselessness of quinine in its treatment, I had come for some years to regard this disease as non-malarial and as one *sui generis*. In 1903, struck by certain features common to trypanosomiasis and kala-azar, I ventured to suggest in the third edition of this manual that the latter disease might be a trypanosoma disease.

A few months later, Leishman published a paper "on the possibility of the occurrence of trypanosomiasis in India" wherein he stated that in 1900, at Netley Hospital, at the *post-mortem* of a soldier who had died of so-called dum-dum fever, he had discovered in smear preparations from the spleen-pulp a number of small round or oval bodies, two or three microns in diameter, which, on being stained, presented besides the nucleus a smaller rod-like chromatin mass, set perpendicularly or at a tangent to the circumference of the larger nuclear mass. At the time he was unable to explain the nature of these bodies; but in May, 1903, on coming across similar bodies in the blood of a rat which had died of nagana and the blood of which during life contained numerous

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trypanosomes, he surmised that the bodies found in the soldier in 1900 represented degeneration forms of trypanosomes.

In July, 1903, Donovan stated that he had found similar bodies three months previously in smears of the spleen, taken *post-mortem* from cases said to have died from chronic malaria. On June 17th, he found identical bodies in splenic blood taken during life from a patient suffering from irregular fever and enlarged spleen, and whose peripheral blood showed no malaria parasites. Identical bodies had also been found by Marchand in January, 1903, in sections of the spleen, liver, and bone marrow from a patient who had taken part in the Pekin campaign and had suffered from a long continued irregular fever, extreme enlargement of the spleen and anæmia.

In December, 1903, having under treatment a patient from Darjeeling suffering from typical kala-azar, I had the opportunity of examining blood abstracted from his spleen on two occasions, and found it swarming with the peculiar bodies already described by Leishman, Donovan, and Marchand. I was able to show that these bodies were not endo-corpuscular parasites, as suggested by Laveran and Mesnil, who had expressed the opinion that they belong to the genus *Babesia*.

Then followed observations by a number of investigators, and we learnt that kala-azar was a widely distributed, though hitherto unrecognised disease. It was found in various parts of the eastern side of India, in Ceylon, China, Arabia, the Soudan, Algeria, Crete and South Africa. Besides those of Leishman and of Donovan, amongst the most important papers on the subject are those of Christophers, who showed that the parasite attacks the endothelial cells; of Leonard Rogers, who in cultivating the parasite obtained a characteristic, flagellated form; of Dr. J. H. Wright, of Bostorf, U.S.A., who found parasites morphologically indistinguishable from those of kala-azar in the granulation cells of tropical sore; of James, who confirmed and extended Wright's observation; of Patton, who considers he has discovered

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the extracorporeal developmental forms of the parasite in a species of bed bug and of Nicolle and Comte on the occurrence of the same or a similar parasite in children and dogs in Tunis.

Epidemiology.—Our knowledge of the epidemiology of kala-azar is gathered mainly from the Assam epidemic, which began about 1870, when the disease appears to have been introduced from Rangpur. Rogers believes that it was possibly a continuation of a similar epidemic known as "Burdwan fever" which had been raging in Lower Bengal. The importation theory is supported by the names of "Sirkari disease" and "Sahib's disease" given by the Garos, who state it was unknown among them until after the English took over their country. The epidemic began almost simultaneously at Bengal Kutta and Karaibari, two places fifty miles apart but in direct communication with the Rangpur district. The epidemic advanced very slowly along the valley of the Brahmaputra, taking seven years to spread less than a hundred miles. Following the lines of intercourse, it attacked first the larger stations, and then spread to the smaller villages around. The introduction of the disease into a village was almost invariably traced to someone coming with the disease on him from an infected locality. Some isolated villages escaped in a remarkable manner. Whilst the disease spread up the valley, the invasion of new places was counterbalanced by its dying out in villages and districts which had previously suffered. Generally, it clung to a place for about six years, and then disappeared without any apparent change in the local conditions. A house appeared to retain the infection for many months; the natives considered that it could not be re-occupied with safety under one year. During the course of the epidemic, kala-azar never extended far above the level of the Brahmaputra valley. The disease did not arise in the first instance in the interior of the Garo Hills district, as some authors advanced, but appeared first at the foot of the hills, and then spread between them along the patches of low, flat, terai country.

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On account of its deadliness, especially in the smaller villages, kala-azar as it swept onwards became a terror to the natives. Those suffering from the disease were turned out of the villages; sometimes they were made unconscious with drink, taken into the jungle, and burnt to death. Some villages cut off all communication with neighbouring villages for fear of infection; others deserted their homes and even migrated to a different district.

Although the foregoing is the only recorded example of kala-azar as a widespread and active epidemic, it had been recognised that a disease clinically identical occurred sporadically in several places in India and elsewhere. These cases had often been regarded as a form of malarial cachexia, but the identity of the sporadic and epidemic disease has now been established by the detection of the Leishman or Leishman-Donovan body in both.

Ætiology (*see* Frontispiece).—The kala-azar parasite, according to Rogers, belongs to the genus *Herpetomonas* Légér. We know two stages of this body, intracorporeal and extracorporeal. Possibly these represent respectively asexual and sexual forms; the former found in man and possibly in some other vertebrates, the latter obtained in artificial cultural media, and, it may be, in certain insects—flies, bugs.

The distribution of the parasite within the body of man is very general. Apparently its special habitat is the endothelial cells of blood-vessels and lymphatics. In those large mononucleated cells it has been found in the spleen, in the liver, in the bone marrow, in the lung, in the kidney, in the mesenteric glands, in petechiæ, in the arachnoid, in ulcers involving the intestinal mucosa, and in papules and ulcers of the skin. It occurs also in the blood, though in small numbers, being found there both in polymorphonuclear and mononuclear leucocytes, very rarely in the red corpuscles. In the blood it is in greatest abundance towards the termination of the case, especially during fever, and when intestinal symptoms are present (Donovan).

The "Leishman" or "Leishman-Donovan body,"

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as it is generally called, is a small ovoid or roundish organism measuring from 2 to 4 $\cdot\mu$ in diameter. Stained according to Leishman's method, it shows two lilac-coloured chromatin masses, one larger than the other, enclosed in a cytoplasm which acquires a faint bluish tint about the periphery. The larger chromatin mass is the nucleus, which may be oval and centrally placed (resting stage), or elongated and at the periphery (pre-division stage). The smaller chromatin mass is the micronucleus or blepharoplast; it is usually in the shape of a short rod, and is placed perpendicularly, or at a tangent to the nucleus. It stains more deeply than the latter. The parasites multiply by simple fission, the division of the body being always preceded by the elongation and division of the nucleus and blepharoplast. The plane of division is always longitudinal. Some forms suggest a

Fig. 49.—Kala-azar parasite from the spleen, stained.

process of multiple fission, attaining a larger size, becoming almost circular and presenting as a rule six chromatin masses, three large and three small, the former being placed round the periphery.

The parasites, as they occur in man, are probably almost invariably intracellular. They grow and multiply within the host-cell, causing it to enlarge, and then, after disintegration of the nucleus, to disrupt. The parasites so set free either enter other endothelial cells, or are taken up by the white blood corpuscles, in which they are sometimes found in the peripheral circulation. In smear preparations they are often free or in clusters of various numbers, sometimes arranged with great regularity like the merozoites in the segmenting quartan or tertian malaria parasites. Sometimes as many as 50 or 200 parasites are found together embedded in a structureless matrix

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or stroma, probably the remains of the original host-cell.

In cultures, the parasites enlarge very rapidly. They retain at first their shape, the cytoplasm becoming granular, opaque and vacuolated. Having attained a diameter of 7 to 9 μ, they assume an elongated piriform shape and become flagellated. The flagellum arises from the blepharoplast at the rounded end of the parasite, and projects at once clear of the body as in *Euglena*. There is never an undulating membrane as in trypanosomes. These flagellated

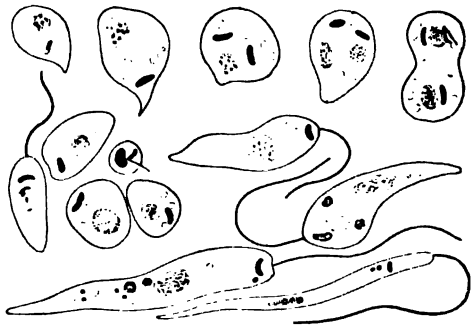

Fig. 49A.—Kala-azar parasites in cultures. (*After Leishman.*)

forms measure from 12 to 20 μ in length. They multiply by longitudinal fission; sometimes throwing off exceedingly fine linear forms (Leishman), comparable in their delicacy to spirilla.

The culture medium used by Rogers was blood to which a small quantity of sterile, slightly acid citrate of soda solution was added to prevent coagulation. When the culture medium was kept at blood heat, the parasites very rapidly degenerated and disappeared; but when placed in an incubator at 27°C. they lived for three or four days and multiplied. A lower temperature was found to be even more suitable. When temperature was lowered to 20°—22°C., the parasites multiplied more readily, acquired a considerable size, and finally assumed the elongated, motile, flagellated form.

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Hitherto all attempts to transmit the parasite to vertebrates have failed.

Under natural conditions kala-azar, like other diseases caused by similar protozoal organisms, is probably transmitted by a living agent, possibly a biting insect or tick. There are certain facts, however, which tend to suggest that the carrier of the kala-azar infection need not necessarily be a blood-sucking animal. In the first place, the asexual stage of the parasite in man is not in great abundance in the peripheral circulation. Secondly, the parasite is often present in ulcerations of the skin and of the intestinal mucosa, suggesting elimination by these organs. Thirdly, we know that although some species of *Herpetomonas* are fostered by blood-sucking flies, such as *Tabanus* and *Hæmatopota*, others are found in non-biting forms, such as *Musca*, *Sarcophaga*, *Pollenia* and *Fucellia*, which could become infected only by settling on ulcerations or on fæcal matter. It is conceivable that such insects might transmit the infection by depositing the parasites on wounds and abraded surfaces. Recent observations by Patton seem to indicate a certain species of bug as a transmitter. In this insect, after feeding on kala-azar patients, he found flagellated forms like those in cultures. If this important discovery be confirmed it affords an explanation of the tendency of the disease to cling to particular houses, and supplies a valuable guide in directing prophylaxis.

Predisposing causes. — Kala-azar attacks both sexes and all ages, but, *unlike malaria*, it shows a predilection for the acclimatised—the natives and old residents; in them it is said to be as severe and fatal as in the case of newcomers.

Incubation period.—This is difficult to fix. In the case of one Englishman, recently under my care, the time that elapsed from his arrival in perfect health in the endemic region and the onset of the fever which terminated in kala-azar (diagnosed microscopically both before and after death), was under ten days.

Symptoms.—Bentley, speaking from a large

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experience and with full knowledge of the literature of epidemic kala-azar, says that the disease commences with high fever, which may be preceded by rigor, and, in some cases, by vomiting. This initial fever—intermittent in some instances, more frequently remittent—may be very severe. It lasts for from two to six weeks, occasionally longer. During its progress the spleen and liver enlarge, increasing and decreasing at first, often in a most remarkable degree, in harmony with the fluctuations of the fever. Then comes a period of apyrexia and general improvement, to be followed once more by fever and splenic and hepatic enlargement, and perhaps tenderness. In this way spells of fever and apyrexia recur for months, absolutely unchecked by quinine or other drugs, until finally a low form of fever, rarely over 102°, becomes more or less persistent. Profuse sweats are common during remissions at all stages of the fever; rigor is rare. Pains in the limbs often suggest rheumatism. When the disease is thoroughly established emaciation and anæmia become noticeable, and, together with the enlargement of the liver and spleen, cause the patient to present a typical appearance. Œdema of the legs, sometimes circumscribed œdemas, or even ascites may now be present. In many the skin acquires an extraordinary earthy-grey colour; the hair is apt to become dull, dry, and brittle, and may fall out; petechiæ, in the axillæ especially, are not unusual; epistaxis and bleeding from the gums are common. This condition of chronic fever, enlargement of spleen and liver, emaciation and anæmia, may continue for months, or even one or two years, until improvement sets in, or, more usually—96 per cent. of cases (Rogers)—until the patient is cut off by intercurrent disease, especially dysentery (90 per cent.), occasionally phthisis, pneumonia, or asthenia.

According to Rogers, the degree of anæmia, in uncomplicated cases, is usually only a moderate one, the number of red corpuscles being not in frequently over 4,000,000, and, as a rule, over 2,500,000 even in advanced cases. The most re-

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markable change in the blood is the great and constant reduction in the number of leucocytes. Instead of there being one white to about 625 red, as in a normal subject, the proportion is commonly from one to 2,000 to one to 4,000, and may be lower still. The reduction is most marked amongst the polynuclear variety; the lymphocytes and large mononuclear leucocytes, although greatly reduced in number, show a relatively increased percentage as in other protozoal diseases.

In those cases which I have had an opportunity of carefully watching I have been struck with the fact that, notwithstanding the chronic fever and progressive wasting, throughout the long illness the tongue has been almost uniformly clean and the appetite and digestion good.

Morbid anatomy.—The *spleen* is greatly enlarged and may show signs of perisplenitis on the thickened capsule. The trabeculæ are enlarged, the pulp increased in bulk and full of blood. A section or smear preparation, appropriately stained, will show prodigious profusion of parasitic growth in the crowds of the large mononuclear cells already referred to. The *liver* also is generally much enlarged. It has a brown or mottled section. The parasites are in great abundance, occupying large mononuclear cells, attached or free, in the dilated hepatic and portal capillaries. There may be some cirrhotic changes, but the hepatic cells, though atrophied and perhaps fatty, never contain parasites. The *bone marrow* is similarly packed with parasite-laden cells. *Intestinal ulceration* is very common, and parasites may be found in the walls of the ulcer as well as in *skin ulcerations* or in the *lymphatic glands*. Occasionally they are found in connection with the blood-vessels in the *kidneys*, but never in the epithelium of the secreting tubules.

Diagnosis.—Irregular chronic fever with enlargement of the spleen and a relative mononuclear leucocytosis suggests kala-azar. An examination of the blood can at once exclude leucocythæmia and, if taken together with absence of tertian or quartan periodicity

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and the inefficacy of quinine, malaria. Trypanosomiasis or kala-azar may be difficult to distinguish, and unless their respective parasites are detected a positive diagnosis is impossible, although geographical considerations and subsidiary skin and lymphatic lesions may assist in forming an opinion.

Banti's disease clinically approaches very closely, and can only be excluded by a microscopical examination of the liver and spleen juices, or of the blood. Similarly, malignant disease of the abdomen, so often associated with irregular chronic fever, in the absence of a satisfactory microscopical examination of liver or spleen juice, may be difficult to distinguish from kala-azar.

On the discovery of the germ cause of kala-azar, and the fact that this disease is widely distributed throughout the tropics and sub-tropics, there was at first a tendency to regard all cases of febrile tropical splenomegaly other than those associated with malaria, trypanosomiasis and other well-known conditions, as kala-azar. Further observation and experience have considerably modified this view, since it has been found that a proportion of such cases do not show the Leishman body, either during life or after death. Possibly other protozoal germs, as yet unrecognised, are responsible for some of these cases. So that, in any given case of tropical splenomegaly, until the Leishman body is found it would be rash to pronounce a positive diagnosis of kala-azar.

The discovery of the Leishman body in the blood or tissues, therefore, is the only reliable indication of kala-azar. In the first instance it should be sought for in the blood, and especially in the leucocytes, after appropriate staining. A high power immersion lens is indispensable, and every leucocyte must be carefully scrutinised for the little oval body with the round or oval nucleus and rod-shaped blepharoplast. Several films must be searched in this way before recourse is had to splenic or, better, as being less dangerous, hepatic puncture.

Splenic puncture must not be lightly undertaken. Death from hæmorrhage has frequently followed

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what might seem a trivial procedure. When the liver is enlarged, being a less vascular organ and less easily torn, it should be selected for punctures in preference to the spleen. The abdomen had better be fixed firmly with a binder to prevent as far as possible movement of the diaphragm and consequent risk of tearing the punctured organ. A fine hypodermic needle, scrupulously clean and dry, should be used, the patient being directed not to start or breathe while the puncture is being made. Failure to draw blood is not to be regarded as failure to obtain material for microscopic examination; on the contrary, it is an advantage, as the object is to procure spleen or liver pulp, not blood. After blowing out the contents of the needle on a slip, a film should be spread and, after it has dried, stained by Leishman's or Geimsa's procedure, and then examined with a twelfth objective. The parasite is easily recognised by its shape and two chromatin masses.

Treatment.—This, as a rule, is most unsatisfactory. Intercurrent malarial attacks may be treated with advantage with quinine, but for the disease itself this drug, even in huge doses and persisted with for long periods, is useless, if not harmful. Arsenic has proved equally unsatisfactory.

I have recently treated four cases with intramuscular injections of atoxyl. In two of these there was no improvement, the disease running its usual fatal course; but in the other two cases recovery has ensued, whether as a result of the treatment or not I cannot assert. The atoxyl should be given as for trypanosomiasis, best, according to my experience in Europeans, in three-grain doses every three days and persevered with for a year or longer. The expulsion of intestinal parasites, change to a healthy climate, good food, warmth, rest, physical comfort, and good hygienic conditions are indicated.

Prophylaxis.—Having regard to the character of the disease, it seems to me that in the endemic districts the cases should be dealt with as infectious, that they should be isolated, and that their houses and fomites should be disinfected or burnt.

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Oriental sore and kala-azar—If the parasite of oriental sore be specifically identical with that of kala-azar, it must somehow have been deprived of its virulence; for, although kala-azar is a fatal disease, oriental sore is eminently benign. It is known that one attack of oriental sore confers immunity against further attacks of the same disease. Oriental sore is a disease of camel-using countries. It is said to affect dogs and possibly other animals. May it not be that the virulence of the Leishman body is removed by passage through the camel or some other animal; or, possibly, by being transmitted by some intermediary other than that which transmits the virulent kala-azar? If this be so, we have at hand a vaccine against kala-azar. The idea is worth testing: "Are those who have had oriental sore immune as regards kala-azar, and *vice versa?*"

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CHAPTER XII

RELAPSING FEVER

Synonyms.—Febris recurrens; spirillum fever; famine fever; tick fever.

Definition.—An acute infectious disease, or, possibly, a group of infectious diseases, characterised by fever of sudden onset and, after several days (1 to 7), rapid subsidence, and which may relapse at intervals of from one to seven or more days for an indefinite number of times. It is caused by spirochætæ which are present in the blood during the fever and are transmitted by certain insects (bed bug, body louse) or by certain ticks (Argas, Ornithodoros).

Geographical Distribution.—Relapsing fever is found in Europe, Asia, Africa, America and probably in Australasia. In Europe it occurs in Britain and, especially, in Ireland; also in Norway, Denmark, Germany, Russia and Turkey. In Russia there have been many epidemics; it attacked the Grand Army in the retreat from Moscow, the allied armies in the Crimea, and, also, the armies of both sides in the Russo-Turkish war. In Africa the disease has long been known in Egypt, the Soudan and Algeria. Recently Philip Ross, Milne and Cook found it in Uganda, Dutton and Todd in the Congo Free State, Wellman in Angola, and Koch in German East Africa. In Asia relapsing fever is known to occur in China, in Sumatra, and in India, where Carter's classical investigations were made. In America it was recognised in the United States in 1844; in 1869 it was epidemic in New York and Philadelphia. It is probably widely distributed throughout South and Central America.

From the symptoms, as far as they are known and from the fact that they are communicated by tick bite, we are justified in conjecturing that the

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carapata disease described by Livingstone and Kirk as endemic in the Zambesi basin, the miana disease of Persia, and a similar disease described by Alleman in Mexico may be spirochæta-produced diseases, possibly forms of relapsing fever.

History.—Relapsing fever was known to Hippocrates. He describes an epidemic which he witnessed on the island of Thasos. Among other cases, he quotes those of two brothers, in one of whom the initial paroxysm lasted seven days, in the other six; the intermission in one was five days, in the other six; the relapse in both lasted five days. He further mentions the splenic enlargement, the jaundice, the liability to abortion in pregnant women, and the tendency to menorrhagia. From the time of Hippocrates onwards there is no further notice of relapsing fever in medical literature until 1770; in that year Rutty in his book on the diseases of Dublin described it.

In 1873, Obermeier discovered the spirochæta of relapsing fever. In 1897, Tictin stated that the parasite and the disease were communicated by the common bed-bug; he infected a monkey with relapsing fever by subcutaneous injection of blood obtained from the stomach of a bug which had previously fed on another monkey inoculated with the disease.

Lastly, Philip Ross and Milne, in 1904, in Uganda, and, rather later, but independently, Dutton and Todd on the Congo, discovered that in Africa the spirochæta was communicated by the bite of a tick, *Ornithodoros moubata*. The last two observers found that the parasite could pass into the egg and larva and so confer infective powers on the mature tick of the succeeding generation.

Ætiology.—Experiments on monkeys have proved that one form of relapsing fever is caused by *Spirochæta recurrentis*. This is a delicate spiral filament (7 to 9μ by 0.25μ) provided, as shown by appropriate staining (Loeffler's whip stain) with a long flagellum (5 to 7μ by 0.1 to 0.2μ). The body of the parasite may have three, four or six bends or turns, the flagellum from

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three to five. By the Romanowsky method the body of the parasite usually stains uniformly, with the exception of the extremities, which are pointed and take only a very faint tint. In fresh blood, the spirochæta, propelled by the flagellum, exhibits very active screw like movement. Some are longer than others, the long forms resulting from end to end attachment of two or more parasites. That this is the explanation of the long forms, which may measure from 16 to 100μ, is shown by staining. In those measuring from 16 to 19μ we find a flagellum at each end of the filament and a pale zone in the middle, the pale zone corresponding to the approximated lightly staining extremities above referred to. The still longer forms admit of a similar explanation.

Obermeier and von Jaksch describe certain refractile bodies present in the blood during the fever intermissions. The last-named author says that he has observed the development of these bodies into short rods from which the typical spirochætæ are eventually evolved. This observation has not been confirmed.

Opinions differ as to the biological nature of the spirochæta—whether it belongs to the bacteria or to the protozoa. Novy and Knapp (*Journal of Infectious Diseases*, 1906), who regard it as a bacterium, point as evidence to (*a*) the pale zones in the stained long forms as possibly indicating transverse division; (*b*) the spiral arrangement and very delicate nature of the flagellum, so unlike in these respects that of the flagellata; (*c*) its not being killed rapidly and disintegrated by the slow addition of water to the blood; (*d*) its not being provided with an undulating membrane or being attracted as the trypanosomes are by air bubbles in microscopic preparations, the trypanosomes in such circumstances arranging themselves around the bubble, their flagella pointing inwards; (*e*) its uniform staining; (*f*) absence of nucleus and blepharoplast. In favour of the protozoal nature of the spirochætæ are (*a*) the presence of an undulating membrane but no flagella in certain species, as for example *S. plicatilis and S. refringens;* (*b*) the elements constituting a long spiral are all of approxi-

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mately the same length, which is that of the individual spirochæta; (*c*) the parasites are not all of the same thickness, some being twice the diameter of others, facts suggesting a longitudinal, that is protozoal, rather than a transverse or bacterial method of division; (*d*) the parasite keeps alive for many days—40—in the body of the bug; (*e*) at least in the case of the African form, it enters the egg of the tick *in utero*; (*f*) it is communicated by an arthropod; (*g*) that it has not been cultivated.

Schaudinn propounded the view that the leucocytozoon of the owl (*L. ziemanni*), after fertilisation in the gut of the mosquito, gave rise to an enormous number of trypanosome-like forms which he regarded as spirochætæ. These he considered were a flagellated stage of an intracellular organism and, therefore, belonged to the protozoa. He stated that he had compared his mosquito-bred flagellates with *S. recurrentis* and *S. anserinum*, and that he found they agreed completely in morphological character with what he considered the spirochæta stage of *L. ziemanni*. Before his death Schaudinn seems to have modified his opinion, for in a later paper he states that *L. ziemanni* is far removed from the typical spirochætæ such as *S. recurrentis*.

Novy and Knapp claim that their observations on the cultivation of trypanosomes in the blood of birds which, so far as microscopical examination went, appeared to be free from these organisms, show that Schaudinn, probably unconsciously, worked with mixed infections; and that the trypanosomes which he regarded as a stage in the life of the intracellular *L. ziemanni* were not in any way related to the spirochætæ, but merely a trypanosome derived either from birds or from trypanosomes of the mosquito, which is itself very liable to this type of infection.

Different Species of Relapsing Fever parasites.—Having had the opportunity of examining the blood of a patient from Gibraltar suffering from her eighth paroxysm of relapsing fever, I suggested, on the ground of the unusually large number of relapses and the locality in which the infection was acquired, that there might

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be several forms of this type of disease, due to different species or varieties of spirochætæ. In 1905, in the discussion following the reading of Dutton and Todd's paper on tick fever (Brit. Med Ass., 1905), Sambon made a similar suggestion, basing it on the wide geographical distribution of relapsing fever, the apparent clinical differences of the disease in different places, and the diversity of animals believed to transmit the infection. Koch points out that in African tick fever the febrile stages are shorter (under three days) than in European relapsing fever, and that the spirochætæ in the blood are comparatively scanty; similar observations have been made by Philip Ross and Dutton and Todd. Novy and Knapp, in comparing specimens of spirochætæ from European and

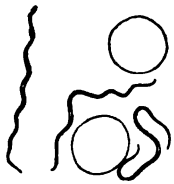

Fig. 50.—Spirochæta duttoni.

African cases, noted that the spirochætæ of the African disease are twice as long (16μ) as the classical *S. recurrentis*, and, moreover, that the former has a tendency to dispose itself in figure of eight coils or in perfect circles. The Indian species they also incline to regard as distinct. The latter, like *S. recurrentis*, measures about 8μ, but is apparently thinner and more flexible, forming less regular spirals, which, moreover, vary in width. Like the spirochætæ of African tick fever, it, too, has a tendency to form loops.

For the African species Novy and Knapp propose the name *S. duttoni*; *S. carteri* would be an appropriate name for the Indian species. Such a nomenclature can only be regarded as provisional: the evidence as yet is far too limited to warrant its permanent adoption; the recent elaborate experiments of Todd and Breinl have shown that the immunity conferred

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through infection with the spirochætæ of Indian relapsing fever does not protect against the African form, and *vice versâ*, thereby proving that, at least pathologically, they are distinct forms.

Mode of transmission.—I have already referred to the Persian disease called miana fever, and to the carapata disease of the Zambesi valley, as possibly being forms of relapsing fever. They are certainly communicated by ticks, *Argas persicus* in one case, *Ornithodoros moubata* in the other. Marchoux and Salimbeni were the first to show that a similar disease of fowls caused by the *S. gallinarum* is transmitted by a tick, the *A. miniatus*, which Neumann pronounces to be identical with or a mere variety of *A. persicus*. The relapsing fever of Europe, and possibly that of India, has been supposed to be conveyed by the common bed-bug, *Acanthia lectularia*. Proof of this is by no means complete. Breinl, Kinghorn and Todd, notwithstanding repeated attempts, failed to communicate the disease by means of these insects. But as we have now reason to believe that there are several species of pathogenic spirochætæ producing disease in man, it may be that these observers have not worked either with the appropriate species of spirochæta, or with the appropriate species of Acanthia. Thus may we explain the positive results claimed by Sikiel, in Odessa, and by other Russian experimenters. There can be no doubt from the experiments of Philip Ross and Milne in Uganda, and Dutton and Todd on the Congo, that the African species, *S. duttoni*, is normally conveyed by the tick *Ornithodoros moubata*, and that it can be transmitted not only by the animal that has bitten the infected individual, but by its progeny. Symptoms of successful infection by the tick appear in from five to seven days.

Animal experiments.—It is generally stated that *S. recurrentis* can be transferred only to man and monkey. Novy and Knapp infected white mice and white rats. The former they found were specially susceptible, the organism appearing in the blood within 24 hours of inoculation and persisting to the

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third day (80 hours). About this time they disappear for several days from the blood of the infected mice and until the commencement of relapse. The first relapse may be followed by a second, third, or even a fourth, the number varying in individual mice; with each relapse the parasites reappear in the blood. The interval between the relapses, counting from the first appearance of spirochætæ in one to their first appearance in the next relapse, is generally about seven days; occasionally it is only two; occasionally it is as long as ten days. The number of spirochætæ in the relapses is much smaller than in the first paroxysm, clearly indicating the development of a partial immunity. Recovery in mice, as with other animals, is the rule.

The same observers found rats to be susceptible, but in them the progress of the disease was different. The period of incubation was longer (40 hours), and there were no relapses. As a result of the consecutive passage of the spirochætæ through a long series of rats its virulence was augmented, so that the incubation period became reduced to 15 or 18 hours, and the persistence of the parasite in the blood prolonged to 60 hours instead of, as originally, 48 hours; at the same time the spirochætæ became far more abundant.

The parasite, which is present not only in the circulating blood but in all the organs, seems to produce no serious pathological change in the rat beyond great temporary enlargement of the spleen. Recovery is practically invariable. Young rats are more susceptible than old rats. Immunity persists for many months.

Rabbits and guinea-pigs are refractory.

Immunity.—Sabritschewsky in 1896 showed that when equal parts of spirochæta-infected blood, or serum, and normal serum are mixed, the spirochætæ survive longer than when the infected blood is mixed with that of an individual who has recovered from relapsing fever. He accordingly concluded that the cause of the crisis in relapsing fever and of subsequent immunity was the development of a germicidal substance in the blood. He was the first to apply serum-

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therapy in the treatment of relapsing fever. He obtained an anti-spirochæta serum by repeated inoculation of the horse with human spirochæta-containing blood. The value of this serum was successfully established by Löwenthal; of 87 patients treated, 43 (47 per cent.) recovered without a relapse.

Novy and Knapp have proved the presence of a powerful germicidal substance in relapsing fever blood by comparing the viability of the spirochætæ in blood taken (1) at the onset of the disease, (2) during crisis, (3) 12 to 24 hours after disappearance of parasites, and (4) from animals hyperimmunised by repeated infection. In the case of the first (1) the spirochætæ live and are mobile for 40 days, and the blood will continue infective up to 37 days: in the case of the second (2) no living spirochætæ are to be found after 24 to 48 hours; in the third (3) the parasites die in from 30 to 60 minutes; in the last (4) they are killed instantaneously.

They further showed by examining the blood during the decline of the fever in an infected animal treated with immune blood that the presence of agglutinating and germicidal bodies could be demonstrated *in vivo* from hour to hour. The parasites are seen to form agglutination rosettes and long agglutination filaments of 70 to 100μ.

Treated *in vitro* with hyperimmune serum the spirochætæ rapidly become unrecognisable aggregations of granules.

Incubation period.—The incubation period usually lasts from two to ten days. In some instances the attack develops promptly on exposure; it is never delayed beyond the fourteenth day. In the artificially inoculated, symptoms show themselves in from two to six days.

Symptoms.—*European and Indian type.*—The onset is generally abrupt, being marked by chilliness or rigor, giddiness, vomiting and intense headache. In the young there may be convulsions. Temperature rises rapidly to 104°F. or 105°F., sometimes even to 108°F. The pulse is rapid, 110 to 130. Should fever run high, there may be delirium. The skin

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is dry, although, especially during the first day, occasional sweats may break out. A slight icteric tinting of the conjunctiva is usual; not infrequently jaundice is marked. The spleen is invariably enlarged and tender. The tongue is coated and moist except in bad cases, in which it may become dry and brown. The bowels, as a rule, are confined. Occasionally herpes labialis is noted, and in certain epidemics a rash of rose-coloured spots on the trunk and limbs has been observed. Some authors describe petechiæ. A slight bronchitis is not uncommon. The urine, not appreciably diminished in amount, is very high-coloured. This, the primary fever, lasts for from five to seven days. At first, the morning is usually lower than the evening temperature, but on or about the third day the evening temperature rarely rises above that of the morning. On the fourth, fifth, or sixth day there is again a rise of temperature, sometimes with delirium, ending in crisis of profuse sweating and diarrhœa. The temperature now falls rapidly to normal or sub-normal, sometimes dropping in the course of a few hours as much as ten degrees; in the latter event, especially in elderly or delicate patients, there may be dangerous collapse.

The initial pyrexia, called *first paroxysm*, is followed by a *first period of apyrexia* during which the patient recovers so rapidly that after four or five days it may be difficult to keep him in hospital. But from seven to nine days after the crisis, that is about the fourteenth from the commencement of the attack, rigor again occurs, followed by a second attack of fever—*first relapse*. This may be more severe than the first paroxysm; usually it is milder and seldom lasts so long. During its continuance the secretion of urine is considerably increased; sweating also is profuse and prostration marked.

With the defervescence of the first relapse the patient enters on the *second period of apyrexia*, which is usually coincident with convalescence. But in some patients a *second relapse* may occur, usually about the twenty-first day counting from the commencement of symptoms. This second relapse rarely lasts longer

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than three days, and is generally milder than the previous paroxysms. In rare instances three, four, five, or even more relapses have been observed. Convalescence may be protracted, and complicated with such sequelæ as nephritis, ophthalmia, otorrhœa, pneumonia, neuritis, parotitis, adenitis. In pregnant women abortion is the rule.

African type.—The African tick-conveyed spirillum fever, although as regards the type of fever resembling the classical European and Indian forms, differs from these in some important particulars. The initial fever is not usually so prolonged, generally terminating in crisis within three days. Diarrhœa and dysenteric symptoms are not uncommon. The apyretic intervals are of very irregular duration, being, according to Philip Ross, sometimes as short as one day, sometimes as long as three weeks; and instead of only one or two relapses, as in ordinary relapsing fever, there may be as many as eleven, five or six relapses being the rule. The fever, though shorter, is as severe in the relapses as in the initial paroxysm, but the intervals tend to become longer. In some instances the reverse is the case, perhaps in both particulars. Sometimes the fever may assume a low chronic form, it may be with severe headache and vomiting. Iritis is not an uncommon complication or sequela. As already stated, the parasites are usually very scanty in peripheral blood and may be hard to find.

In the natives of the endemic districts the disease, as generally observed, is not nearly so severe as in Europeans and strangers, being usually limited to a paroxysm or two of one or two days' duration. The mildness of these attacks is probably explained by a partial immunity conferred by previous attacks.

Mortality.—The death-rate is usually below six per cent. In the feeble and old death may take place at the height of the first paroxysm.

Diagnosis.—This disease is readily confounded with malaria, enteric, typhus and influenza. The detection of the spirochætæ with the microscope, or by animal injection, is the most reliable method of

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diagnosis. At an early stage, the relapsing character of the clinical phenomena, not having declared itself, is not available as an aid to diagnosis, but at a later period the history of a fever which had relapsed about fourteen days from the commencement of the disease should be regarded as highly suggestive of relapsing fever.

Morbid Anatomy.—The spleen is usually large and soft. Livor, kidneys, and heart show cloudy swelling. The skin in fatal cases is usually jaundiced, and there may be submucous petechiæ. The bone marrow is hyperæmic. There is generally a marked polymorphonuclear leucocytosis.

Treatment.—Until serumtherapy is available the treatment of relapsing fever must be conducted on general principles. We know of no drug which can cut short the disease or prevent relapse.

Serumtherapy.—Novy and Knapp have proved that active immunity follows recovery from spirochæta infection, and that this immunity can be increased to a remarkable degree by successive injections of spirochæta-infected blood. They have further shown that passive immunity can be imparted by the injection of recovered or of hyperimmunised blood, and that both active and passive immunity persist for months. Preventive inoculations have been successfully practised in rats, mice and monkeys. Infected animals can be promptly cured by the injection of hyperimmunised serum, and relapses can be prevented by the same means. Although Todd has not been so successful in similar experiments, it seems probable that we have in these observations a basis for the prevention and cure of relapsing fever in man.

Prevention.—The fact that the spirochæta is conveyed to man by bug or tick bite indicates that personal and domestic cleanliness and the avoidance of people and places infested with such vermin must form the basis of successful prophylaxis. Especially to be avoided in Africa are the resting places of caravans and travellers, and the huts of natives.

The mosquito net, a bed well off the ground, and a night light are indispensable in that country, where the nocturnal habits of *Ornithodoros moubata* render the hours of sleep especially dangerous.

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TICKS.

Recent developments in human and veterinary pathology have shown that ticks play an important part in the transmission of disease. They are widely distributed, almost every animal either having species special to itself or being liable to attack by species of a wider zoological range. They belong to the order of the *Acarina*, of which they are by far the largest specimens. They are always visible to the naked eye, and the females are almost invariably larger than the males. In some species the ovigerous females, when gorged with blood, may reach a length of nearly half an inch. As a rule they are temporary parasites, but some live in a quasi-permanent manner on the body of their host; and, occasionally, a few, as the sheep tick (*Ixodes reduvius*), may even burrow beneath the skin. They differ from insects in possessing four pairs of legs, and in having the three regions of the body, head, thorax and abdomen, fused into one unarticulated mass. This latter feature also distinguishes them from the spiders, in which the abdomen is clearly distinct from the cephalothorax.

After impregnation the female tick attaches herself to her host. Becoming enormously distended with its blood, she drops off and secretes herself in some convenient hiding-place where she deposits her eggs, which are small, yellowish, roe-like grains, amounting in some cases to thousands. Oviposition begins from two to ten days after the host has been quitted, and goes on for several days. In due course (two or three weeks under favourable conditions) the eggs are hatched. The larvæ look like minute moving grains of sand. They are characterised by having only three pairs of legs, no stigmata, and no sexual orifice. A suitable opportunity presenting, the larva attaches itself to its vertebrate host. After a period of growth it goes through a first moult (ecdysis), and emerges from its larval skin as a *nympha*, provided with eight legs instead of six, and with a pair of large stigmata placed, one on each side of the body, behind the fourth pair of legs. After a second period of growth it becomes sexually mature. The nymphs undergo three moults, the third bringing them to the imaginal condition. In some species, as in the case of *Margaropus boris*, the metamorphosis from larva to nymph, and from nymph to imago, takes place upon the same host, the parasite remaining attached during the process. In other species, as in the case of *Hæmaphysalis leachi*, the tick, before each moult, drops off as soon as it ceases feeding, and in consequence has to find a host three times during its life instead of once. Having reached maturity the sexes unite. After fertilisation, the male dies, but the female proceeds to engorge herself with blood for the development of her ova. On account of the difficulty of finding an appropriate host, ticks at all stages are endowed with a phenomenal capacity for fasting. Megnin found *Argas persicus* alive after a fast of four years' duration.

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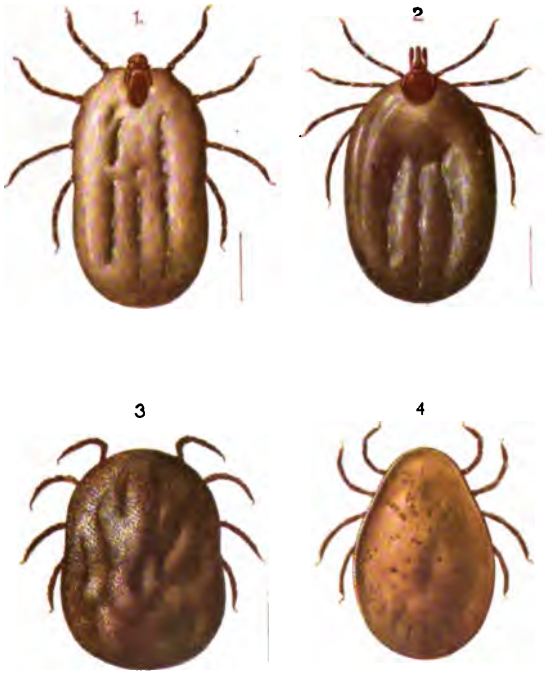

TERZI

PLATE IV.—Ticks (females).

1, Margaropus (Boophilus) annulatus (partially distended); 2, Ixodes reduvius (partially distended); 3, Ornithodoros moubata; 4, Argas persicus.

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Ticks are referable to two families, the *Ixodidæ* and *Argasidæ*, differing both in structure and life habits. Their characteristics and generic classification are indicated sufficiently for practical purposes in the synoptical table on page 205.

The species which are of particular interest to the human pathologist are *Ornithodoros moubata* and *Argas persicus;* the former being the transmitter of the spirochæta of African relapsing fever, the latter of the germ, possibly a spirochæta, of the Miana disease. It is quite likely that other species will in the future be found to be concerned in the transmission of disease germs to man. Important animal diseases due to *Spirochætæ* and *Babesiæ* are also known to have tick transmitters. *Spirochæta gallinarum* of fowls in Brazil is transmitted by *Argas miniatus*. *Babesia bovis* of cattle and deer in Europe is transmitted by *Ixodes reduvius*. *Babesia bigemina* is conveyed in various countries by different species of *Margaropus*, such as *M. annulatus*, *M. australis*, *M. decoloratus ; Babesia parva* by *Rhipicephalus appendiculatus* and *R. simus ; Babesia ovis* by *R. bursa ; Babesia equi* by *R. evertsi*, and *Babesia canis* by *Hæmaphysalis leachi* and *Dermacentor reticulatus*.

Ornithodoros moubata (Murray) (*O. Savignyi* var. *cæca* Neumann) is extensively distributed throughout tropical Africa (Plate IV.). Its body is flattened from above downwards, and is oval in outline. Its colour, when alive, is greenish brown. The integument is hard, leathery, covered with close-set shining granules or tubercles, and marked both above and below with symmetrically arranged grooves. The females may attain about 8 mm. in length by 6 to 7 mm. in breadth. This species is widely distributed in Africa from Uganda and Somaliland in the east, and Congo and Angola in the west, to Namaqualand and the Transvaal in the south.

In habit, *Ornithodoros moubata* resembles the common bed bug. It lives in the huts of the natives, hiding during the day in cracks in the walls and floors, or in the thatched roofs, and moving about actively during the night in search of nourishment. It attacks both man and beast. It feeds slowly, and would be unable to get much blood from any but a sleeping person. Dutton and Todd observed that a big female might remain, firmly fixed, feeding on a monkey for two or three hours before it finally dropped off, distended to the size of a cherry. *O. moubata* deposits its eggs in batches of fifty, seventy or a hundred. Dissection has shown that only a few eggs mature at a time. The fertility of the female is favoured by liberal feeding. The eggs hatch in about twenty days. In the case of this tick, Dutton and Todd have observed that the larval stage is practically omitted. About seven days after oviposition, the hexapod larva can be seen to be forming within the translucent egg-shell. At about the thirteenth day the egg-shell splits, and at about the same time the larval skin splits also, and the eight-legged nymph throws off simultaneously both the egg-shell and its larval skin.

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An interesting feature, and one, perhaps, having a bearing on the ætiology of tick-transmitted diseases, pointing as it does to a channel by which the eggs may receive a germ ingested by the parent, concerns certain cells in the stomach wall. The tick, while feeding, from time to time expels *per anum* a whitish material. This excretion is derived partly from the Malpighian tubes, and partly from the cells alluded to. In the stomach wall, nourished by the imbibed blood, these cells elongate towards the cavity of the ventricle, the other end, smaller and becoming clavate, splits and emits the elaborated nutriment into the general body cavity, where it mixes with the blood of the tick. The cell then becoming globular drops into the lumen of the stomach, constituting part of the white excretion expelled *per anum*. One can readily understand how, by the former route, a parasite could reach the tissues of the tick, including the ovaries.

O. moubata is especially common along the routes of travel. The rest-houses are always the most infested. The ticks are frequently carried long distances in mats or bedding, or in porters' loads, which had been piled for safety in the rest-huts at night.

The natives, and also the Boers, protect themselves in some parts by plastering their huts, both floors and walls, with mud and cowdung. The huts are also frequently smoked in order to drive the ticks from the thatch. A most valuable remedy for immediate use is the powder of the pyrethrum flower, which should be dusted between the sheets of the bed. Some protection may be obtained by keeping a lamp alight by the bedside throughout the night.

In certain parts of Africa the distribution of *O. moubata* is overlapped by that of a closely allied species, **O. Savignyi**, which has also similar habits. *O. Savignyi* differs from *O. moubata* in being provided with eyes, in having larger processes on the legs, and a more minutely pitted dorsal surface. *O. Savignyi* has been recorded from Egypt, Nubia, Abyssinia, Somaliland, British East Africa, etc. It also may be concerned in the transmission of African relapsing fever or other disease. Its bite is dreaded by the natives.

Argas persicus (Fischer), (Plate IV.), has a flat, thin oval body of a yellowish, greenish or reddish colour, spotted on the back with a great many white granulations. The legs are pale yellow. It is found in the north and east of Persia, also in Syria, Turkestan, Russia, China, Algeria and Cape Colony. It attacks both poultry and human beings. Its habits are similar to those of *Ornithodorus moubata*; it infests old houses, living in the cracks of walls and floors. Kotzebue says that in Persia it may so infest villages as to drive out the inhabitants.

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GENERIC CLASSIFICATION OF TICKS

Rostrum terminal. *Dorsal Shield* present. *Ambulacra* present.

Family IXODIDÆ

IXODINÆ

Ventral Shields cover entirely ventral surface of ♂. *Anal groove* surrounds anus anteriorly. *Eyes* absent. *Rostrum* long.

Palpi long and channelled in ♂ and ♀. *Dorsal Shield* of ♂ does not cover body entirely. *Stigmata* oval in ♂, circular in ♀. *Tarsi* without terminal spure. *Grooves* in ♀ dorsally 2 long ones; ventrally 2 bell shaped, 1st with apex at vulva, 2nd with apex at anus. — **IXODES.**

Palpi long, conical, not furrowed in ♂, slightly furrowed and claviform in ♀. *Stigmata* round in ♂ and ♀. *Anal groove* indistinct in ♀. Parasitic on Birds. — **CERATIXODES.**

Palpi pyriform and not furrowed in ♂, claviform in ♀. *Stigmata* circular in ♂ and ♀. *Legs* very long. Parasitic chiefly on Bats. — **HÆMALASTOR. (ESCHATOCEPHALUS).**

RHIPICEPHALINÆ.

Ventral Shields—2 adanal shields on ventral surface of ♂, frequently other accessory shields. *Anal groove* surrounds anus posteriorly. *Eyes* present. *Rostrum* either long or short.

Rostrum base (dorsally) hexagonal forming on each side a projecting angle. *Ventral Shields* in ♂ 2 large triangular or rectangular adanal plates, and frequently 2 smaller ones placed externally to the former. 1st *Coxæ* bidentate.

Anal grooves present—*Marginal festoons* quite distinct in ♂ and young ♀. *Palpi* flat on dorsal surface and with external margin straight or convex. *Stigmata* comma-shaped, with tail long in ♂, short in ♀. *Dorsal Shield* sometimes marked with light spots. External adanal plates shorter than internal. — **RHIPICEPHALUS.**

Anal grooves and *Marginal festoons* absent. *Palpi* with external margin of 2nd and 3rd joints thicker towards the middle and forming outwardly acute angle. *Stigmata* circular. *Dorsal Shield* dark brown. External adanal plates as long as internal. — **MARGAROPUS (BOOPHILUS).**

Rostrum long. *Body* elongate-oval. *Colour* deep brown. *Ventral Shields* in ♂ 2 large triangular peri-anal, and 2 small posterior plates. *Stigmata* comma-shaped, with tail long in ♂, and short in ♀. — **HYALOMMA.**

AMBLYOMMINÆ.

Ventral Shields absent. *Anal groove* surrounds anus posteriorly. *Eyes* often present. *Rostrum* either long or short.

Eyes present. *Rostrum* base broader than long. *Palpi* short and thick. *Stigmata* comma-shaped. *Dorsal Shield* ornamented. 1st *Coxa* bidentate in ♂ and ♀. — **DERMACENTOR.**

Eyes present and conspicuous. *Rostrum* long. *Stigmata* usually triangular. *Dorsal Shield* often with coloured ornamentations. *Marginal festoons* in ♂ nearly always present. — **AMBLYOMMA.**

Eyes absent. *Rostrum* base pentagonal. *Stigmata* comma-shaped. *Dorsal Shield* covers dorsum entirely, shorter than broad in ♀, usually marked with green spots. Parasitic on Snakes and Lizards. — **APONOMMA.**

Eyes absent. *Rostrum* base rectangular, twice as long as broad. *Palpi* conical, 2nd joint with lateral well-marked conical projection. *Stigmata* comma-shaped or circular. 1st *Coxa* non-bifid. 4th *Coxa* in ♂ presents well-developed spur. — **HÆMAPHYSALIS.**

Rostrum concealed by overlapping cephalothorax. *Dorsal Shield* absent. *Ambulacra* absent.

Family ARGASIDÆ

Body usually flat with thin edges. *Ventral grooves* absent or very shallow. *Eyes* absent. — **ARGAS.**

Body with thick edges. *Ventral grooves* present. *Eyes* sometimes present.
- A movable sclerite on each side of the palpi — **ALECTOROBIUS.**
- No movable sclerite on each side of the palpi — **ORNITHODOROS.**

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CHAPTER XIII

YELLOW FEVER

Definition.—An acute, specific, very fatal febrile disease occurring epidemically, or as an endemic, within a peculiarly limited geographical area. Though subject to great variations, its typical clinical manifestation may be said to be characterised by a definite course consisting of an initial stage of a sthenic nature, rapidly followed by an adynamic condition in which such evidences of blood destruction as black vomit, albuminuria, and hæmatogenous jaundice are liable to occur. One attack generally confers permanent immunity. The germ is transmitted by the domestic mosquito, *Stegomyia fasciata.*

Geographical distribution.—Of all the important zymotic diseases, yellow fever has the most restricted geographical range. Its centre is the West Indies, whence it spreads north to the United States and Mexico; south to the Brazils and, at times, as far as Buenos Ayres and Monte Video; west to Central America, and across the Isthmus of Panama to the Pacific coast, along which it extends north to the Gulf of California and south to Peru. It occurs also, in the epidemic form, on the west coast of Africa. Whether it is endemic in Africa it is impossible to say; neither is it now possible to determine from existing records whether it was originally an African or a West Indian disease.

Yellow fever has been imported frequently into Portugal and Spain, and once from Spain into Italy. Although a good many died in these visitations, the disease has never obtained a permanent footing in Europe. Cases have occurred in seaport towns in France and England—Brest and Swansea, for example; these little epidemics, however, have invariably rapidly died out.

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In several of the West India islands yellow fever is endemic. Until recently it was always to be found in Havana. Formerly the Brazils enjoyed an absolute immunity; but ever since 1849, when yellow fever was introduced for the first time into Bahia by a ship from New Orleans, it has been practically endemic in the large cities. At Rio de Janeiro, although in some years the cases are few, it is never entirely absent. In such places as New Orleans, Charleston, Monte Video, and Buenos Ayres, although now and again epidemics of great severity break out, several years may pass without its appearing. Some of these epidemic visitations bring a heavy death-bill; thus in New Orleans, in 1853, 7,970 people died of yellow fever; in 1867, 3,093; in Rio, in 1850, it claimed 4,160 victims; in 1852, 1,943; and in 1886, 1,397. In Havana the annual mortality from this cause used to range from 500 to 1,600 or over.

Epidemiology.—*Influence of atmospheric temperature.*—The histories of these and other epidemics show that the virus of yellow fever can be transported from one place to another, and that for its development in epidemic form it requires an atmospheric temperature of over 75° Fahr. It ceases to spread when the thermometer sinks below this point, and it stops abruptly as an epidemic when the freezing-point is reached. Dampness favours yellow fever; it is therefore most prone to occur and to spread during the rainy season.

Usually a sea-coast disease.—The favourite haunts of the disease are the sea-coast towns, the banks of rivers, and flat delta country. Rarely does it pass far inland, or ascend high ground. Still, there are many exceptions to this general rule; for yellow fever has been found far inland, and at a considerable elevation (São Paulo, Brazil, 2,500 feet; Newcastle, Jamaica, 3,000–4,000 feet; Cuzco, Peru, 9,000–10,000 feet). Villages are seldom affected; nor does the disease readily spread if introduced into rural localities. In spreading inland it follows the lines of communication—railways, canals, navigable rivers.

A ship disease.—Ship epidemics were common

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occurrences formerly. The ideal haunt of yellow fever is the low-lying, hot, squalid, insanitary district in the neighbourhood of the wharfs and docks of large seaport towns.

A place disease.—It is, in a sense, a place disease like malaria and beriberi. That is to say, if the patient be removed to a hitherto unaffected spot, his attendants and neighbours will not contract the disease, unless the spot itself first become infected. The occurrence of this place infection will depend on whether the particular locality affords the appropriate intermediary—the stegomyia mosquito—for the transmission of the germs brought by the patient. If the locality supplies this condition, then, for the time being, the disease will spread and become epidemic; if the locality does not supply this condition, then the disease will not spread. It is safe, therefore, to visit a yellow fever patient if he is lodged outside the endemic or epidemic area; but it is never safe for the susceptible to visit the endemic area, whether they come into direct contact with the sick or not.

Immunity acquired by prolonged residence or by a previous attack.—A well-established fact about yellow fever is that the natives of, and those who have lived for a long time in, the endemic area are practically immune from the disease; or, if they are attacked, the disease is usually of a very mild type. It is also said that if the native quits the endemic area his immunity decreases in proportion to the length of time he remains away; so that after long absence, on his return to the endemic area he may be attacked just as an ordinary visitor might be. Further, those who enter the endemic area for the first time are the most susceptible, the susceptibility decreasing with length of residence. It is probable, therefore, that at such places as Rio the endemicity of the disease is kept up by the continual influx of foreign and, therefore, susceptible visitors.

Race as influencing susceptibility.—Formerly it was believed that the negro is little liable to yellow fever, and that when he gets it the attack is usually mild; and, also, that the yellow-skinned races are more susceptible

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than the negro, but less so than the European. It was also said that the susceptibility of the European increases in proportion to the height of the latitude of his native place; that is, the Norwegian is more susceptible than the Frenchman, and the Frenchman more than the Italian or the Spaniard. The facts on which this belief was founded may admit of another and more rational explanation than that of varying degrees of racial susceptibility; relative racial susceptibility may be more a matter of racial opportunity than of colour of skin.

Incubation period.—The incubation period of yellow fever rarely exceeds four or five days; it may, it is said, be much shorter—under twenty-four hours. The limits, according to Bérenger-Féraud, are one to fifteen days in the temperate zones, one to thirty days in the tropics. Precise experiments indicate an average incubation of from three to five days, and an extreme limit of thirteen days. Occasionally it happens that the disease breaks out in a ship after she has been several weeks at sea, having had no communication with the land or with another ship in the meantime. The rationale of this, and also of the prolonged incubation periods formerly assigned by writers to the disease, we now understand. It must not be inferred from these ship epidemics that the incubation period is to be reckoned in weeks. The virus may have been in the ship from the time she left port, but the crew may not become infected until long afterwards.

Incubation period preceding epidemic extension.—It has been observed that a period of at least a fortnight elapses between the arrival of a yellow fever patient in a hitherto uninfected district and the occurrence of the first case of the epidemic he may give rise to. That is to say, that although, as stated above, the incubation period of yellow fever—the period elapsing between the introduction of the virus into the body and the on-coming of fever—is usually only from three to five days, yet a period of at least twelve days must elapse before that virus after removal from one human body can be effectively implanted in another human body. What becomes

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of it during these twelve days? The answer to this question has now been supplied, and with it the key to most of the epidemiological peculiarities of yellow fever.

Duration of the infective period.—This is singularly brief. A yellow fever patient is dangerous to his neighbours only during the first three days of the disease. After this he cannot confer infection.

The germ.—A great many attempts have been made to discover the germ or virus of yellow fever, and a corresponding variety of organisms have been described. In the belief that some of these were the true germs of the disease, certain bacteriologists went the length of practising protective inoculation with attenuated cultures of their respective organisms, whilst others elaborated curative sera on the orthodox lines. Both sets of enthusiasts have claimed successes. We now know, however, that the germ of yellow fever is not a bacterium, at all events is not a visible bacterium, and that it cannot be cultivated or modified on the ordinary bacteriological lines. Freire's *Cryptococcus zanthogenicus*, Finlay's *Tetragenus febris flava*, and Sanarelli's *Bacillus icteroides* have no longer anything but an historical interest.

At the instigation of the Government of the United States, these and other organisms were rigidly investigated by Sternberg, whose standing as a bacteriologist and whose judicial cast of mind eminently qualified him for forming a trustworthy judgment. His verdict on them, and on many similar organisms for which pathogenic claims had been advanced, was unfavourable.

Nature of the yellow fever germ indicated by epidemiology.—In earlier editions of this book I remarked, "The reasons for the peculiar geographical limitation of yellow fever are but partially understood. A principal reason, undoubtedly, is that yellow fever belongs to a somewhat restricted class of diseases which, though communicable, are not directly so through immediate conduction from sick to sound; diseases whose germs do not pass quickly from the sick to the healthy, like those of scarlatina and

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smallpox, but have first, apparently, to undergo extracorporeally developmental changes that enable them to attack, and to live in the human body. Such diseases, seeing that their propagation demands an additional condition—the extracorporeal state or medium—must necessarily be more difficult to acquire, must spread more slowly, and be more limited geographically, than the ordinary infectious diseases." These remarks, suggested by the peculiar epidemiological features of yellow fever, have received remarkable confirmation by the brilliant work of Reed, Carrol, Agramonte and Guiteras, and by many subsequent workers.

The germ occurs in the blood. — This Reed, Carroll, and Agramonte have incontestably demonstrated. They injected into six non-immunes blood from yellow fever patients. In this way, in five instances, they conferred the disease within the recognised limits of the incubation period. In another experiment they induced yellow fever by injection of defibrinated blood. By other experiments they showed that the virulence of the blood was destroyed by a temperature of 55° C. Another point, already alluded to, is that these experiments, taken in conjunction with others to be presently described, showed that the germ is present in the blood, at all events in a transferable state, only during the first three or four days of the disease. Yet another point these experimenters sought to establish, viz. that this phase of the yellow fever germ is so minute that it can pass through a Berkefeld filter. Further, that blood from a yellow fever infection produced by injection of filtered serum will, on being injected into another non-immune, again confer the disease; proving that the virus so conveyed was capable of multiplying, not a toxin merely, but a living germ. These latter inferences are deduced from what was practically only one experiment. Although the evidence, therefore, is somewhat meagre, yet, considering the high order of the other work accomplished in the same field by these American observers, we are almost justified in concluding with them that, like

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the germ of rinderpest, of horse-sickness, of foot-and-mouth disease, and Durham's dysentery bacterium, at least one phase of the yellow fever germ as it exists in the blood, though particulate, is ultra-microscopic.

The mosquito the intermediary and diffusing agent of the germ of yellow fever.—Having satisfied themselves by direct observations and by a long series of carefully-conducted culture experiments on the blood, that the germ of yellow fever was not of an ordinary bacterial nature, guided by the epidemiological considerations detailed above, and encouraged by the recent discoveries in the ætiology of malaria, the American observers thought that possibly, as in malaria, the mosquito was an essential factor in the life cycle of the yellow fever germ, as Finlay had conjectured many years before. After some preliminary experiments, which unfortunately proved fatal to Dr. Lazear, one of the original members of this courageous band of observers, carefully planned systematic attempts were made to convey yellow fever by means of the bite of the common West Indian mosquito, *Stegomyia fasciata*. Twelve non-immunes, who had had no opportunity of contracting the disease from other sources, were bitten by mosquitoes previously fed on yellow fever patients. Of the men so bitten, ten (83·3 per cent.) developed the disease within the normal incubation limits — three to five days. Subsequently Guiteras, repeating this experiment, obtained a positive result in eight (47 per cent.) out of seventeen non-immunes bitten.

The germ not transferable by recently-infected mosquitoes.—As might have been partly expected from the blood inoculation experiments already described, it was found that it was only mosquitoes that had fed during the first three days of the fever that were infective. It was further demonstrated that the germ must undergo in the mosquito some necessary developmental process, for it was not until twelve days had elapsed after feeding on yellow fever blood that the experimental insects could convey infection. Repeated trials made with mosquitoes two to ten

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days after they had so fed always gave negative results; whereas the same insects rarely failed to infect when set to bite non-immunes at any time subsequent to the twelfth day after their yellow fever blood meal. It was also proved that they retained their infective power for at least fifty-seven days.

These experiments fully explain—1st, the impunity with which a yellow fever patient can be visited by a non-immune if outside the endemic area; the mosquitoes in the vicinity are not infective. 2nd, the danger of visiting the endemic area, especially at night; the mosquitoes there are infective and active. 3rd, the discrepancy between the incubation period, three to five days, of the disease, and the incubation period, fourteen days and over, of an epidemic; the necessary evolution of the germ in the mosquitoes infected by the original introducing patient demanding the space of time indicated by the difference between these two periods. 4th, the clinging of yellow fever infection to ships, buildings, and localities; the persistence of the germ in infected mosquitoes (*Stegomyia fasciata*) which are known to be capable of surviving for five months and probably longer, after feeding on blood. 5th, the high atmospheric temperature required for epidemic extension of yellow fever; such temperature favours the activities and propagation of the mosquito, and is probably necessary for the evolution of the germ also in the mosquito.

Since the announcement of these discoveries many independent observers and several commissions have studied yellow fever in its relation to the mosquito, but beyond confirming the results of the original American observers and adding some facts in the bionomics of *S. fasciata*, there has been no great addition to our knowledge of the subject. The germ itself is still unrevealed.

Marchoux and Simond have given us several new facts about the yellow fever germ. They have shown that, although it is arrested by the Chamberland bougie B, it can pass bougie F; that it will not infect if simply laid on a raw (blistered) surface; to

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secure infection it must be injected subcutaneously; that virulent blood serum loses its virulence in forty-eight hours, if exposed to the air at 24° to 30° Cent., but if protected by oil or vaseline it will retain its virulence for five days.

As regards *S. fasciata*, the same observers note that to lay eggs she must first have a feed of blood, and that her eggs are deposited about three days after she has so fed. Before the first egg-laying, *S. fasciata* is both diurnal and nocturnal in her feeding habits, biting at any time; subsequently she is strictly nocturnal in this respect. Therefore a stegomyia that bites during the day does not convey yellow fever. She is too young; any parasite she may harbour is immature. In this way is to be explained the impunity with which a yellow fever centre may be visited during the day, although the visitor may be bitten by stegomyia. Europeans who live at Petropolis, a suburb of Rio de Janeiro, and are in the habit of visiting and transacting their business in the low-lying yellow fever-haunted districts of the city, never contract the disease unless they are so imprudent as to pass the night in the latter.

The parallelism between the ætiology of yellow fever and that of malaria is very complete, and encourages the conjecture that the germ, like that of malaria, is of a protozoal nature; that as a result of a sexual process it undergoes growth and development in the mosquito; and that the sporozoites resulting from this process are emitted in the salivary secretion of the infected mosquito when, at any time subsequent to the completion of the developmental process, she proceeds to feed on blood. Although the germ of yellow fever as it occurs in the blood may be ultra-microscopic, the analogy of the malaria parasite favours the idea that in the insect it may grow to a visible size, and that although search in the blood for the cause of this grave disease hitherto has proved unsuccessful, it may yet be demonstrated in the tissues of the mosquito. Further, as several species of mosquito of the sub-family *Anophelinæ* have been shown to foster the malaria parasite, it

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is not improbable that several species of the genus *Stegomyia* may turn out to be effective intermediaries for the germ of yellow fever.

Symptoms.—There is the same variety in the initial symptoms of yellow fever as in other specific fevers. There may be sudden rigor supervening in the midst of apparent health; there may be only slight chills; or there may be a period of premonitory malaise leading up to the more pronounced symptoms. When fairly started, the procession of events is rapid.

Roughly speaking, and provided there are no complications, an attack of yellow fever is divisible into three stages: 1, The initial fever; 2, "the period of calm," as it is called; and 3, in severe cases, the period of reaction.

The initial fever lasts usually from three to four days. The maximum temperature is generally attained within the first twenty-four hours, or by the second day, and, in a case of medium severity, may rise to about 103° or 104° Fahr. During the three or four succeeding days the mercury slowly sinks to 98° or 99° Fahr., the daily fluctuations being seldom more than half to one degree. It occasionally happens that high temperature is maintained for two or three days, and also that the maximum is not attained till the third day; as a rule, the thermometer behaves as described, the maximum being reached within a few hours of the onset of the disease.

With or soon after the initial chill or rigor, severe headache sets in, and is generally a prominent feature. For the most part the pain is concentrated about the forehead, in the circumorbital region, and in the eyeballs themselves. In many cases it is associated with intolerance of light.

Loin pain is another very distressing symptom; it may amount to positive agony. The legs, too, ache excessively—particularly the calves, knees, and ankles; they feel as if broken.

The face is flushed and swollen; the eyes are shining, injected, and ferrety; the skin is dry.

What with pain and febrile distress, the patient

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rapidly passes into a very miserable condition. He is restless and continually tossing about.

At first the pulse ranges from 100 to 120, and is full and strong; but, as the disease progresses, the pulse loses its sthenic character, gradually falling in force and frequency until, at the "period of calm," it becomes remarkably slow and compressible, beating perhaps only 30 or 40 times per minute.

At the outset the tongue is not very dirty, but it soon acquires a white coating on the dorsum, the edges remaining clean. It is not so swollen and flabby as in malarial fever; on the contrary, it is rather small and pointed throughout the disease. This is regarded as an important diagnostic mark; taken along with the progressive diminution in the strength and frequency of the pulse, and the peculiar behaviour of the temperature, it is nearly conclusive as to the disease being yellow fever. Later, the tongue dries, and, at the same time, thirst becomes intolerable. The palate is congested and swollen; the gums may also swell and bleed.

The congested appearance of the face at the onset of the disease tends to subside; so that by the time the asthenic stage is reached the features may have become shrunken and small, the eye sunken, and the eyelids discoloured by ecchymoses.

In some cases the skin is hot and dry throughout; in others it may be bedewed with perspiration from time to time; or the sweating may be constant, especially so if collapse sets in.

By the third day the scleræ assume a yellowish tinge, and very often the skin acquires the yellow colour from which the disease derives its name. It must not be understood, however, that every case presents this colour of skin; in some it is entirely absent, but if carefully looked for there is always some yellowness of the scleræ to be discovered. The yellow tinging of the skin generally shows about the end of the first stage, deepening in intensity as the case advances, and remaining apparent for a considerable time after convalescence has become established. It ranges in depth from a light saffron

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tint to a deep mahogany brown. In fatal cases it is always present; not necessarily during life, but invariably after death. The skin in bad cases is said to emit a peculiar odour like gun washings, or, as Jackson puts it, like the smell of a fish market.

Petechial, erythematous, papular, and other eruptions may show themselves in different cases; but in yellow fever there is no characteristic eruption, unless it be an erythematous congestion of scrotum or vulva, which occurs in a proportion of cases and is said to be diagnostic.

An important feature, from the diagnostic as well as from the prognostic point of view, is the appearance, in some cases almost from the outset of the disease, of albumin in the urine, together with a tendency to suppression. In mild cases these features may be little marked; but in severe cases, particularly during the stage of depression, the urine may fall to a few ounces, and be loaded with albumin to the extent of one-half or even two-thirds. The more pronounced these symptoms, the graver is the prognosis. Urea and uric acid are very much diminished, the former in severe cases falling to 1·5 gramme to the litre. The urine is almost invariably acid. Bile pigments show themselves towards the end of the disease; their appearance is regarded as a favourable omen. Hæmorrhage from kidneys or urinary tract is not uncommon.

Delirium may occur, but is not an invariable feature. Usually, after the initial stage of restlessness and acute suffering, the patient becomes torpid, and perhaps taciturn. In bad cases coma, subsultus, etc., may gradually supervene, the temperature rising as death approaches and even after death.

At the outset the bowels are confined. In the second stage, diarrhœa, perhaps of black material resembling the vomit, may supervene; or there may be actual hæmorrhage of bright red blood from the bowel.

The well-known *black vomit*—always a grave symptom, but fortunately not by any means an invariable one—forms one of the most striking features of this disease. In the earlier stages of the fever

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vomiting of bilious matters is a common occurrence. This may subside, or, after a time, give place to a coffee-ground vomit which gradually deepens in colour until it becomes uniformly black. On microscopic examination the vomited material is found to consist of broken-down blood corpuscles and altered hæmoglobin suspended in a yellowish mucoid fluid. This material is, doubtless, in the main derived from blood transuded through the walls of the capillaries of the mucous membrane of the stomach. It is intensely acid. Though the black vomit may not always be seen in fatal cases during life, it is invariably found in the stomach on *post-mortem* examination.

Sometimes pure blood is thrown up from the stomach; similar passive hæmorrhages may take place from almost any part of the body—from eyes, ears, nose, mouth, bladder, uterus, and so on.

Death may occur during the early acute stage, being preceded by a rapid rise of temperature.

In mild cases the "period of calm," which sets in after the subsidence of the initial fever, may last for several days before convalescence is established. In such, recovery once begun is usually very rapid; in a week from the beginning of the disease the patient may be about again. In severe cases, however, the period of calm is followed by a third stage, the stage of reaction, in which the temperature again rises, though not to so high a point as in the initial fever, and a sort of remitting fever of an adynamic type keeps on for several days or weeks. This secondary fever is more prolonged if there is any complication, such as abscess, boils, parotitis, buboes, hepatitis, and so forth. The icterus is now very pronounced; black vomit may recur, or appear for the first time; perhaps a profuse diarrhœa ends in collapse; or the urine may be suppressed, stupor, coma, and other nervous symptoms ensuing, and very often ending in death. In other instances the secondary fever terminates in a crisis of sweating and a prolonged convalescence.

Relapse may occur at any time up to two or three weeks after the subsidence of the initial fever. It is

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specially prone to occur if the patient has been guilty of any dietetic imprudence during the period of calm —a period at which the appetite may return to some extent. Relapses are very dangerous.

Prognosis and mortality.—Prolonged initial rigors, algidity, convulsions, suppression of urine, coma, hæmorrhages are all unfavourable symptoms. The prognosis is good if the temperature during the initial fever does not exceed 103° to 105° Fahr. It is better for women (although, if pregnant, abortion is almost invariable) and children than for men; better for old residents than for newcomers; worst of all for the intemperate. According to a table of 269 carefully observed cases given by Sternberg, there were no deaths in 44 cases in which the temperature did not rise over 103°; *per contra*, in 22 cases in which the thermometer rose over 106° there were no recoveries. Of 36 in which the temperature rose to between 105° and 106°, 22 died; of 80 with maximum temperatures between 104° and 105°, 24 died; and of 87 in which it ranged between 103° and 104°, only 6 died. The mean mortality in the whole 269 cases was 27·7 per cent. Although in some epidemics it has risen as high as fifty or even eighty per cent. of those attacked, the foregoing may be taken as a fairly representative mortality in yellow fever among the unacclimatised—something between twenty-five and thirty per cent. Among the permanent inhabitants of the endemic districts the case mortality is very much lower—seven to ten per cent. During epidemics abortive and ambulatory cases occur; in these, icterus and other characteristic symptoms are often absent. Such cases may be hard to diagnose from febricula or mild malarial attacks. In them the mortality is nil. Some epidemics are particularly mild; in others the majority die. In the same epidemic the cases may vary in severity from time to time. In children the mortality is insignificant.

Pathological anatomy.—Depending probably on hæmoglobin diffused in the liquor sanguinis and tissues, and not on biliary pigment, the yellow colour

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of the skin is most marked in the dependent parts of the cadaver, especially in those parts which are subjected to pressure. Petechiæ are common in the skin; more considerable extravasations of blood may be found in the muscles. The brain and meninges are hyperæmic, and may be studded with minute hæmorrhagic effusions; like the other tissues of the body, they are stained a lighter or deeper yellow. The blood in the vessels of the general circulation is not firmly coagulated. The blood corpuscles appear to be normal, although there can be little doubt that there is in this disease a liberation of hæmoglobin, arising, possibly, from destruction of a proportion of the corpuscles. An important fact, as explaining the liability to passive hæmorrhages, is the existence of a fatty degeneration of the capillaries and smaller blood-vessels. The stomach, as stated, always contains more or less black material, such as may have been vomited during life, and the folds of the gastric mucosa are swollen; here and there are arborescent patches of congestion, and ecchymoses. Observers are not agreed as to the nature of this congestion, as to whether it is passive or inflammatory. Sternberg says that in the increase of leucocytes in the submucosa there is evidence of a slight inflammatory action. The small intestine may contain a dark, acid material similar to that in the stomach, and doubtless coming from the same source. Like that of the stomach, the mucous membrane of the intestine shows patchy arborescent injection.

As compared with other fevers, in yellow fever the liver is characteristically affected. As a rule, if death has occurred at the later stages, this organ is somewhat exsanguine, friable, and presents a yellowish colour from profound fatty changes in the cells. Occasionally, though rarely, it may be hyperæmic and dark. Throughout the gland the cells—particularly those about the periphery of the lobules—on microscopical examination are found to contain globules and grains of fat. The nuclei in some instances, as well as the protoplasm of the cells,

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show fatty changes; the latter may be completely disintegrated. This profound fatty degeneration of the liver cells is well marked in the great majority of cases. It is not confined to the liver. Although most marked in the liver, every organ of the body is more or less affected in the same way.

The spleen is not characteristically affected, but the kidneys show signs of parenchymatous nephritis. Hæmorrhagic foci under the capsule and in the cortex are common. The renal epithelium shows cloudy swelling passing on to fatty degeneration and desquamation. The tubules, here and there, are filled with infarcts, either of an albuminoid material or of *débris* of desquamated epithelium, corresponding with the numerous casts which can be discovered in the albuminous urine.

Diagnosis.—The diagnosis of yellow fever is treated of in the chapters on malaria and blackwater fever (pp. 113, 243), to which the reader is referred. Practically, the only two diseases with which severe yellow fever is likely to be confounded are bilious remittent and hæmoglobinuric fever. The difficulties of diagnosis are often very great. There is no clinical feature, so far as is known, which would distinguish a mild attack of yellow fever from an ordinary febricula, nor any pathognomonic clinical sign that would absolutely distinguish a malarial remittent from yellow fever. Probabilities must be weighed in diagnosis when it is based on clinical grounds alone. The only reliable guides are the discovery of the malaria parasite and the characteristic pigment and leucocytic variation in malarial fever, and the determination of their absence in yellow fever; and, when cases come to the *post-mortem* table, the presence of pigment in the viscera in the former, and of extensive fatty degeneration of the liver cells in the latter.

Treatment.—Formerly a much more active treatment than that in vogue at the present day was the fashion for yellow fever. It is now recognised that, as with most specific fevers, the treatment is more a matter of nursing than of drugs.

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Experience has shown that a smart purgative at the very onset of the disease is beneficial. With many castor oil is the favourite drug, but to be of service it has to be given in very large doses—two to four ounces. Others use calomel; or calomel combined with quinine—twenty grains of each. Others, again, prefer a saline. The purgative, whichever be selected, must not be repeated, or, for that matter, given at all if the patient is not seen until after the second day of the disease.

Hot mustard pediluvia, frequently repeated during the first twenty-four hours, the patient and bath being enveloped in a blanket, are much in favour. They are said to relieve the cerebral congestion and the intense headache. Very hot baths, with subsequent blanketing and sinapisms to the epigastrium, are also said to have a similarly favourable influence on the congestion of the stomach, which is, undoubtedly, another constant feature of the disease. For high fever, antipyretic drugs, cold baths, iced injections, cold sponging, and the like may be carefully employed. In view of the asthenic nature of the disease, the less depressing measures should be preferred.

Vomiting may be treated with sinapisms and ice pills, or with small doses of cocaine. Morphia is dangerous, and must be avoided. For black vomit, frequently repeated doses of perchloride of iron, ergotine injections, acetate of lead, and other styptics have been recommended. For restlessness, phenacetin or antipyrin is used. When the skin is dry, the urine scanty, and the loins ache excessively, Sternberg recommends pilocarpine.

After the fourth or fifth day the flagging circulation demands stimulants of some sort. Iced champagne, hock, or teaspoonful doses of brandy given every half hour, may tide the patient over the period of collapse. Great care, however, should be exercised in the use of these things; if they seem to increase the vomiting and the irritability of the stomach, they must be stopped at once.

The feeding is an important matter. So long as

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there is fever the patient has no appetite; during this time—that is, for the first two or three days—he is better without food. When the fever subsides appetite may return, and a craving for nourishment become more or less urgent; the greatest care, however, must be exercised about gratifying this untimely appetite. Only the blandest foods, and these only in very small quantities, should be allowed—such as spoonfuls of iced milk or chicken tea. Gradually the quantities may be increased; but, even when convalescence is established, solid food must be partaken of very sparingly, and it must be of the simplest and most digestible description. Indiscretion in eating is a fruitful cause of relapse in yellow fever; and it must be borne in mind that in this disease relapse is exceedingly dangerous. Nutrition may be aided by nutrient enemata.

The Sternberg treatment. — Sternberg has introduced a system of treatment by alkalies which promises well. It is directed principally to counteracting the hyperacidity of the gastric and intestinal contents—always a marked feature in yellow fever. His prescription is 150 grains of sodium bicarbonate and one-third of a grain of mercury perchloride in a quart of water; of this an ounce and a half is given every hour. This, he claims, not only neutralises the acidity of the intestinal contents but increases the flow of urine, the perchloride of mercury tending to check fermentation changes in the alimentary canal. Of 301 whites treated in this way only 7·3 per cent. died, and of seventy-two blacks all recovered. Other encouraging figures have been adduced as to the efficacy of this line of treatment, which is certainly deserving of further and more extended trial.

Prophylaxis.—It is the duty of sanitary authorities in tropical countries, so far as possible, to free of mosquitoes the areas over which they have charge. If this were effectually done everywhere there would be no malaria, no filariasis, and no yellow fever. Although complete extermination of mosquitoes is not to be expected, relative extermination of mosquitoes is worth attempting, and certainly much can be

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attained in this direction by the vigorous use of the now well-known measures. In Havana, by such means, in a very few months the number of mosquitoes was reduced ninety per cent., with, doubtless, a corresponding gain to the community in the diminution of mosquito-conveyed disease.

During epidemic visitations or during exacerbations of endemic yellow fever, non-immunes should, if possible, immediately quit the implicated zone. Above all, the slums and low-lying districts of the town should be shunned. These places should not even be visited; or, if visits have to be made to them, they should be as brief as possible, and not made during the night. The susceptible should avoid sleeping in the lower storeys of houses, and pay great attention to general health, carefully avoiding all causes of physiological depression or disturbance. Sailors must not be allowed on shore.

In every country subject to visitations of this disease the sanitary condition of the towns should be most carefully attended to, especially as they refer to the stegomyia mosquito. All water-tanks and cisterns must be effectually screened by fine-meshed metallic gauze; all puddles and stagnant water abolished; all cases of any kind of fever, no matter how mild they may be or what their nature, must be reported at once to the central sanitary authorities, who should have full powers to promptly screen or otherwise deal with them and the houses in which they are. Delay in recognising the earliest cases of a threatened epidemic, as shown by recent experience in New Orleans, is most dangerous, leading, as it may, to the rapid multiplication of infected centres.

Ships should not be allowed to clear from infected ports, nor to enter non-infected ports during the warm season, without adequate inspection. If, on entering port, yellow fever is found on board, the cases should be isolated in a quarantine hospital where there are no stegomyia mosquitoes, the ship thoroughly cleared of mosquitoes, and the passengers and crew prevented for at least five, better thirteen, days from communicating with the shore,

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or until every risk of conveying infection has passed away.

In the event of the disease appearing in a locality which is not habitually a yellow fever centre, and of which the population is small, an economical plan of dealing with the threatened danger is for the authorities promptly to remove the entire population of the neighbourhood, with the exception of the insusceptible and those in attendance on the sick, and to place the deported population before dispersion in a thirteen days' quarantine camp. Meanwhile, the infected area must be rigidly isolated and its mosquitoes destroyed. In this way the spread of the disease will be prevented.

In the event of yellow fever breaking out in the crew of a man-of-war, the cases, if possible, should be sent ashore, and the ship hurried north or south into cold weather, any mosquitoes which may have found their way on board being at once destroyed.

In the case of the appearance of yellow fever in a large town, the method which was so successfully adopted by Surgeon-Major Gorgas, U.S.A., must be adopted. Funds and authority must be obtained at once. An efficient and adequate sanitary staff must be promptly organised and instructed in their duties. Cases of yellow fever should be immediately reported, and the patients promptly protected from mosquito bite by wire screens. At the same time the systematic destruction of mosquitoes in their breeding-places and in the patients' and neighbouring houses must be rigidly enforced. The infected houses should be carefully sealed up by pasting paper over all the doors, windows, ventilators, chimneys, and cracks, and the fumes of pyrethrum or of burning sulphur—2 lbs. per 1,000 cubic feet of space—or other insecticide, employed to stupefy the insects, which should afterwards be swept up and burned. In this way, in 1901, yellow fever was stamped out in ninety days in Havana, a city where for the previous one hundred and forty years it had held uninterrupted sway. In this way, in 1905, New Orleans was freed from the disease in a much shorter period

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than in any previous epidemic; and in this way Gorgas has made the line of the Panama Canal as healthy as New York. Similar results from similar measures are being obtained in the larger Brazilian ports.

Guiteras has shown, in a practical manner, that yellow fever patients may be admitted to the wards of a general hospital or be nursed in private houses with impunity, provided they are protected by effective mosquito netting from mosquito bite during the first three or four days of their illness.

Portability of the virus in fomites and merchandise.—Until recently it was universally believed that the virus may remain for a considerable time potentially infective in fomites, clothes, merchandise, etc., and in wooden structures (ships). Thus Strain describes an epidemic in São Paulo in which he believed the initial cases acquired the infection from unpacking a box of clothes which had lain at Santos for some time and had been damaged there by damp and sea water. The epidemic of 1893 in the same city he traced to certain cases of machinery which had lain for some months at Santos. On opening the cases the packing straw was found to be damp. Four of the people in the house where the cases were opened got yellow fever within a few days.

Many similar instances have been adduced as conclusive evidence of the portability of the virus of yellow fever in fomites. But the very thorough and carefully conducted experiments carried out in Cuba by Drs. Reed, Carroll, and Agramonte go far to prove that fomites have nothing whatever to do with the conduction of the disease. A small, ill-ventilated, badly lighted wooden hut was erected near Havana during the prevalence of epidemic yellow fever. The fresh and stale fomites of yellow fever patients, in the shape of soiled bedding, clothes, black vomit, etc., were strewn about or stowed away in great profusion in this close hut, and among them, lying on beds that had been occupied recently by yellow fever patients, wearing these patients' soiled night clothes and using their soiled blankets, seven non-immunes (that is white men,

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recently arrived and never previously affected with yellow fever) slept during, in the aggregate, sixty-three nights—from November 20th, 1900, to January 31st, 1901—with absolute impunity.

Immunity of the native as affected by anti-stegomyia sanitation. — The immunity of the native of the endemic areas of yellow fever is usually attributed to an attack in childhood. If yellow fever has been exterminated from Havana and other endemic centres by anti-stegomyia measures, the children are no longer attacked by the disease. It follows that, in the course of one generation, the entire population will become non-immune. Doubtless sooner or later the germ of yellow fever will be introduced again, and then, having a population entirely non-immune to spread in, unless promptly checked, a far more extensive epidemic than ever devastated these places in less scientific days will occur. This can be confidently predicted if it be true that the present immunity of the native depends on an attack of ordinary yellow fever in childhood. I am inclined to think that this explanation does not cover the entire ground; for, if the disease be so mild in childhood as not to be recognisable, how was it that Gorgas stamped yellow fever out in Havana, and how is it that the disease is not in evidence there now? I would suggest that there are two strains of yellow fever virus — one of great virulence, one of little virulence. Specifically the same, they are mutually protective, much in the same way as with vaccinia and smallpox. The immunity of the native and the old resident I would attribute to epidemics of the mild strain of yellow fever, which, could it be recognised clinically, might be used as a vaccine against the more virulent disease.

Introduction of yellow fever into Asia.— There is another important matter in connection with this disease which, in the near future, ought to be made a subject for international consideration. I refer to the possibility of the spread of yellow fever to Asia, the Eastern Archipelago, Polynesia, and East Africa. It has spread in the past to Europe;

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this is a comparatively unimportant matter, as the climatic and hygienic conditions in that continent are not favourable to the stegomyia mosquito, and therefore to the extension of the disease. It is otherwise in this respect, it is to be feared, with Asia. Fortunately, yellow fever, so far as known, has never appeared in the crowded, filthy cities of the East; but, should it ever be introduced there, the favourable climatic conditions, the surpassing filth everywhere, the presence of stegomyia mosquitoes, and the too frequent absence of efficient sanitary machinery will enable it to spread like wildfire in an entirely non-immune population. The probable reason of its non-introduction into Asia is that the trade route from the West Indies to China and India has hitherto not been a direct one, but has passed by a long circuit either to the north or to the south. When the American inter-oceanic canal has been constructed, there will be direct and rapid communication between the present yellow fever centres and Asia. With this more direct and more rapid communication there will arise a corresponding risk of spreading yellow fever into a huge section of tropical humanity which has hitherto enjoyed exemption from one of the deadliest diseases afflicting mankind. An infected mosquito (and *Stegomyia fasciata*, according to Giles, is a good traveller), either shipped by accident or brought on board by some thoughtless or malicious person, could easily be conveyed alive to the shores of Asia, and would suffice to set, so to speak, the whole of the tropical section of the Eastern hemisphere in a blaze. The history of the spread of disease by the rapid methods of modern travel is full of examples that should serve as a warning to our rulers and responsible sanitary authorities. Let us hope that before the Central American canal is completed this important matter will receive the attention it demands, and that due care will be exercised that America does not reciprocate the introduction of cholera from Asia by a return gift of yellow fever.

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GENUS STEGOMYIA.

The members of this group of mosquitoes belonging to the sub-family *Culicinæ* present very distinctive characters. Their ova, instead of being cemented together to form rafts as in other *Culicinæ*, are deposited separately, each being surrounded by small air-chambers. Their larvæ are somewhat elongate, with rudimentary antennæ, and a short stout syphon; they maintain an almost vertical attitude. In the nymphæ the

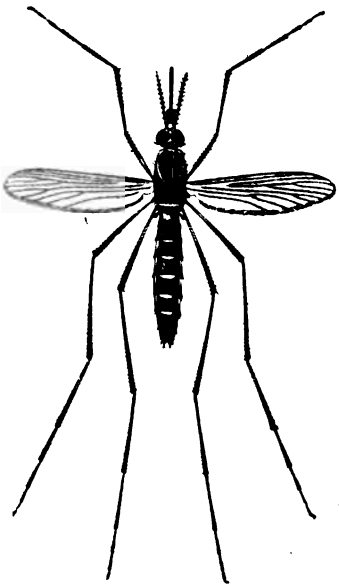

Fig. 51.—Stegomyia fasciata (female).

trumpets are expanded and broadly triangular in shape. The imago exhibits a distinctive scale structure and, at all events in early life, observes diurnal habits.

The *Stegomyiæ* are easily recognised by the broad, flat, imbricated scales which completely cover the head and abdomen and which are invariably present on the middle lobe and frequently also on the lateral lobes of the scutellum. These scales give to the insect a satin-like appearance which is quite characteristic. They are mostly small, black insects, with white, silvery or yellow lines, bands or spots on the thorax and legs. In India they are known as "tiger mosquitoes" on account of their striped appearance. They seem to have a decided preference

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for the littoral, and certain species (*S. fasciata*, *S. scutellaris*) are frequently found on ships and are doubtless distributed by this means. At present, the genus *Stegomyia* includes nineteen species, all of which are easily identifiable on account of their striking thoracic and other ornamentation. Of these the type species, *S. fasciata*, is the most important on account of its wide distribution in all tropical and sub-tropical countries, and because of the part it plays in the distribution of yellow fever.

S. fasciata can be recognised by the peculiar lyre-shaped ornamentation of its thorax, composed of two dull yellow parallel lines in the middle and a curved silvery line on each side.[1] The proboscis is not banded; the abdomen is banded basally; the last hind tarsal joints are all white, and some of the other tarsal joints are marked by light bands basally. This widely distributed species is essentially a domestic form and bites with avidity. It breeds in small artificial collections of water, such as barrels, puddles, cisterns, and even in such small receptacles as sardine tins. The nature of the water appears to be a matter of indifference; it is found equally in rain or waste water, but more frequently in water discoloured by decaying vegetable matter.

Although widely distributed, *S. fasciata* does not occur abundantly in certain parts, such as the Malay States, China, and Africa, where its place is taken by closely-allied species, such as *S. scutellaris* in the Malay States, China, etc., and *S. africana*, *S. argenta punctata* and others in Africa. It is quite possible that, besides *S. fasciata*, other species belonging to the genus *Stegomyia* may be able to transmit the yellow-fever germ.

[1] This ornamentation is constant, but the median thoracic stripes are absent in a variety called *S. fasciata mosquito*.

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CHAPTER XIV

BLACKWATER FEVER

Synonyms.—Hæmoglobinuric fever, melanuric fever, hæmaturic fever.

Definition.—An acute disease characterised by pyrexia, generally ushered in by severe rigor, bilious vomiting, icterus, hæmoglobinuria, and frequently with diminution or suppression of urine.

For a long time this disease, like kala-azar and several other tropical fevers, has been regarded as a form of malaria, and in earlier editions of this manual, in deference to general opinion, I described it, with some reservation, under that head. I have long entertained the idea that too much has been taken for granted in relegating blackwater to malaria, and thereby ignoring its possible individuality as a separate disease; an individuality strongly suggested not only by the symptomatology, but also by epidemiology and analogy. I have therefore now placed it by itself pending definite settlement of one of the most important problems still unsolved in tropical pathology. Such an arrangement, apart from other and more purely theoretical considerations, has its practical advantages.

Geographical distribution.—The geographical distribution of blackwater fever is very wide, but it does not coincide with that of any of the known types of malaria, notwithstanding that in many districts the diseases may be found together. Endemic concurrence must not be looked on as conclusive of identity; the germ causes of very different diseases may have certain topographical requirements in common.

The prevalence of blackwater fever in various countries is most unequal. It is common here and there throughout tropical Africa. It is found all

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along the West Coast from the Senegal to the Coanza, but principally on the Congo and on the deltas of the Niger and Gambia rivers. On the East Coast it is also widely spread, especially along the Zambesi, the lower Shiré, and the shores of the Nyassa. It is far from uncommon in the Upper Niger, in British and German East Africa, in Uganda, in North and South Rhodesia, and in the valley of the Upper Nile. It is also common in some parts of Madagascar. But it is not found in the malarious regions of Lower Egypt, and it is rare in Algeria.

In America it extends over the Southern States of the Union, chiefly Florida, Georgia, Alabama, Mississippi, Arkansas and Texas, but recently it has also been prevalent in North Carolina and Virginia. It is also found in Central America, on the plains of Venezuela and in the West Indies.

In Europe it is restricted to Greece, Sicily and Sardinia. A few cases have been reported from Central Italy. It is extremely rare in the Roman Campagna, the classic land of malaria. In Asia it is reported from Tonquin, the Malay Peninsula, and lately it has been described as occurring in Assam, Darjeeling, the Terai, Meerut and Amritsar. It occurs in many of the islands of the Eastern Archipelago, and also in New Guinea.

Before 1885, strange to say, no Indian writer had mentioned hæmoglobinuria as a feature in the pyretology of Hindustan or of the East. Apart from the possibility of its having been overlooked, there may be another explanation for this singular silence; the disease may have been confounded with bilious remittent. It is difficult to believe, however, that the large number of acute observers who have studied Indian diseases so carefully, and for so many years, could have systematically ignored this striking disease. Possibly, therefore, it is of recent introduction into India. Such an idea is countenanced by the fact that certain medical men practising in Africa, good observers, declare that blackwater fever is of comparatively recent introduction there; and, moreover, that it is yearly becoming more common in that

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continent. In certain States of the American Union it seems to have been only recently introduced. Meek says it first appeared in Texas in 1886.

Topographical distribution. — Although blackwater fever has a wide general distribution, it is limited in its endemicity to low, swampy grounds; and although, as reported by several authors, it sometimes occurs at high altitudes, this does not prove that infection took place there. We know that the disease may remain latent for a considerable time, and that those who have been infected may have relapses at long intervals, and that the clinical manifestations may appear for the first time far from the place in which the infection was contracted. It is a common belief among the older residents in British Central Africa that a change of district, particularly from one level to another, causes blackwater fever, an opinion based on the experience that many cases occur soon after such a change. Amongst Europeans in British Central Africa such changes of district are frequent and as it is only a day's journey from the lowlands to the highlands, it is reasonable to infer that the majority of the cases which occur on the highlands depend on infection contracted previously in the swampy regions at the foot of mountains, and in the season during which the conditions favouring infection are most prevalent.

Seasonal prevalence.—In the Southern States of the American Union blackwater fever is reported to be especially frequent in late summer and in autumn. On the West Coast of Africa it seems to prevail at the close of the rainy season (August and September). For British Central Africa we have no definite information on this point. Like all other infectious diseases, blackwater fever is directly or indirectly dependent on peculiar meteorological conditions. Of course relapses may occur at any season and in any place.

Epidemiology. — Blackwater fever at times assumes an epidemic form. It may not be seen for years in a district, and then numbers of cases may occur within a short time. Very often, as is the

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case in yellow fever, the magnitude of an "epidemic" may depend on the number of susceptible persons, possibly new arrivals, within the endemic region. It broke out amongst the labourers employed in making the canal through the isthmus of Corinth; it attacked the Chinese labourers on the Congo railway; and in 1885, according to Dr. Wenyon, of Fatshan, China, "it ravaged like a plague the Chinese army on the Tonquin border of Kwangsi." In collective dwellings, such as barracks, hospitals, schools, it may attack several persons at the same time. In 1885 it broke out in a prison in Castiades, Sardinia, attacking 24 out of 800 convicts. Sometimes several cases may occur at long intervals in the same house; such houses are known in British Central Africa as "blackwater fever houses."

Predisposing causes.—Individuals of all ages and both sexes are liable to blackwater fever, but they are not equally subject to it. It more commonly affects men about the middle period of life, obviously on account of their greater exposure either to its causative agent or to circumstances provocative of an attack. At one time race was considered an important factor. In Africa, Europeans, Indians, and Chinese are attacked in great numbers, whilst the natives are said to enjoy an immunity. The immunity of the natives is probably not a racial immunity; more likely it is the immunity conferred by infection during childhood. In fact, natives of the same tribe, but living in places which are free from blackwater fever, contract the disease just like Europeans when they come within its reach. Plehn mentions a serious outbreak of blackwater fever among the blacks in the Cameroons, the disease specially attacking those who had come to the coast from the interior. Reynolds says that the disease occurs sporadically amongst the natives of Ashanti.

Among the circumstances which predispose to the active clinical manifestation of the blackwater fever infection, debility from previous illness has undoubtedly a powerful influence. It is usually in those who have suffered from sub-tertian infection or

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dysentery that blackwater fever appears, although cases of the disease in strong, healthy individuals of recent arrival have frequently occurred.

Length of residence.— It has been repeated again and again that Europeans are rarely attacked within the first year of residence in a blackwater fever country, and great stress has been laid on this statement by those who believe that the hæmoglobinuria is not the special feature of a specific disease, but only a symptom of ordinary malaria in people who have previously suffered from several attacks of the prevailing intermittent fever. We know, however, that although in most cases attacks of the more widely-spread sub-tertian may precede blackwater fever infection, yet there are many cases on record in which blackwater fever occurred before any kind of "malaria" had manifested itself. Plehn, Scott, Ritchie, Cardamatis, Lynch, Hearsey, Daniels and others have reported cases of blackwater fever in robust, healthy individuals, who were attacked within two or three months of their arrival in a blackwater fever country. I have frequently been told by officers in the African colonial service that the attack of blackwater fever for which they were invalided, suddenly developed while they appeared to be in perfect health and without any malarial antecedents. Daniels states that few cases occur during the first six months' residence, that they rapidly increase during the next six months, are most numerous during the second and third year, and become rare after five years' residence. This is exactly what might be expected to happen with any localised infectious disease. The relatively small number of cases within the first six months may be explained by non-exposure to the causative agents of the disease; indeed, many arrive in the endemic district at the end of the epidemic season. The progressive prevalence of cases during the first three years finds an obvious explanation in the accumulating chances of infection; the decrease in later years may be partly accounted for by the progressive diminution in the number of the older residents and by the weeding out of the most susceptible. Daniels states that the early

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cases of blackwater fever—those under one year's residence—are mainly (fourteen out of twenty-one) in persons resident at or below the 1,500 feet level; and the majority (ten out of fourteen) of cases in persons having four years' residence, are in persons residing principally in the highlands.

Ætiology.—There are three theories as to the ætiology of blackwater fever: 1, The "malaria" theory; 2, the quinine theory; 3, the specific theory.

1. *The malaria theory.*—The prevalence of blackwater fever in malarious regions, the great frequency of its occurrence in persons who had previously suffered from one or other of the malarial fevers, the finding of malaria parasites and hæmozoin in the blood and organs, and the large mononuclear leucocytosis of hæmoglobinuric cases led to the belief that blackwater fever was an unusually severe form of "malaria." Against this theory is the fact that although blackwater fever is certainly co-endemic with one or other form of malaria in several regions, it is not so in all regions. It has its own peculiar distribution, and is absent or very rare in many places in which the various intermittent fevers are especially rife. It is exceedingly common amongst the few Europeans who live in tropical Africa; it is practically unknown amongst the many thousands of Englishmen who live in the fever haunts of India.

It is quite true that blackwater fever generally occurs in persons who have previously suffered or are suffering from malaria; but this does not prove that it is a special manifestation of malaria. It may be concurrence merely. We do not believe tuberculosis to be a peculiar manifestation of enteric fever because it often follows in the wake of that disease. Moreover, as already pointed out, blackwater fever frequently attacks people who previously had never had a single paroxysm of intermittent fever. The fact that malaria parasites are often found in the early stages of blackwater fever is not surprising when we consider that in many places malaria is exceedingly common and is co-endemic with blackwater fever.

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Although the tertian and quartan parasites have been found in the blood of blackwater fever cases, the parasite which most frequently occurs is the sub-tertian, because it is that species of malaria parasite which is most common in the endemic regions of blackwater fever. Yet of all the intermittent fevers, sub-tertian is the one that differs most clinically from blackwater fever. It is true that sub-tertian varies considerably in different cases; but the type of the disease does not alter, and the number and distribution of the parasites in the organs are always in perfect accordance with the intensity and nature of the various symptoms. In no case of sub-tertian, not even in the most pernicious, do we ever find the symptoms peculiar to blackwater fever. On the other hand, all cases of blackwater fever, however grave, however mild, always exhibit the same characteristic symptoms, with no difference other than as regards intensity and duration. Admitting the malaria theory of blackwater fever, we should have to consider a mild relapse of blackwater fever to be an unusually severe attack of sub-tertian; an untenable paradox. When malaria parasites are found in cases of blackwater fever they may be very scanty and in no way proportional to the symptoms of the disease. But in many cases no parasites are found; or, what is still more striking, if there were a few parasites before the attack, they invariably completely disappear with the onset of blackwater fever, and may not return after recovery from the latter disease. In analogy with what is sometimes observed in pernicious cases of sub-tertian fever, some authors have suggested that the parasites, though scarce or even absent in the peripheral blood, may be numerous in some internal organ, particularly the brain. Against this *à priori* argument are the absence of cerebral symptoms during the attack, and the occasional negative evidence of *post-mortem* findings.

Much has been made of the large mononuclear leucocytosis present in this disease as a proof of its malarial nature. But we now know that a similar type of leucocytosis occurs in several other forms of protozoal disease.

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If blackwater fever be caused by any one of the known malaria parasites, this parasite must have acquired its peculiarly powerful hæmolytic properties in a previous passage through an as yet unrecognised mammalian or insect host; or, the subject of blackwater fever must have been exposed to some specific influence present in blackwater fever countries, but absent in other malarial districts.

2. *The quinine theory.*— The quinine theory of blackwater fever arose in Greece. It was first suggested by Verétas in 1858, and soon became popular amongst Greek physicians. In 1874 it was upheld by Tomaselli in Italy, and quite recently, it has received the support of Koch. The idea that quinine might produce blackwater fever originated from a misinterpretation of the fact that the administration of quinine, even in small doses, may provoke the manifestation of blackwater fever in a patient in whom the infection is latent. As quinine, even in toxic doses, never produces blackwater fever in healthy people or in malaria patients elsewhere, its peculiar action in Africa had to be explained by a peculiar hypothetical idiosyncrasy — an idiosyncrasy which, curiously enough, is found only in certain malarious countries and not in others. Thus, the connection between quinine and blackwater fever is not one of cause and effect, but merely one of coincidence. Blackwater fever was known long before the introduction of cinchona bark into Europe, indeed it was known in the days of Hippocrates. Besides, even recently, numerous cases of blackwater fever have been reported amongst Europeans who had never taken quinine. Cardamatis mentions thirty-two such cases. Then, again, a number of physicians have administered quinine in large doses for the treatment of blackwater fever and have greatly vaunted its beneficial action. Quinine, undoubtedly, provokes in some the clinical manifestation of blackwater fever infection. So, and probably much more powerfully, do chill and fatigue. But no one will contend that the latter cause the disease. Why then attribute it to quinine, which, logically, has no stronger claim?

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3. *The specific theory.*—In 1893, in a paper read before the Epidemiological Society, I stated that, on account of its peculiar symptoms and geographical distribution, I believed blackwater to be a disease *sui generis*. In 1898, Sambon suggested, because of the striking analogies that its distribution, course, symptoms and morbid appearances have with the hæmoglobinuric fevers of cattle, horses, dogs and sheep, that blackwater fever might be a form of babesiasis. This view, which has been adopted quite recently by Blanchard and others, deserves consideration. It is quite reasonable to expect to find in man parasites belonging to this genus of the hæmoprotozoa, so abundantly represented amongst the animals most intimately associated with him. Certainly of all the diseases of man, the ætiology of which is still obscure, none could be more appropriately ascribed to this group of parasites. The analogies between the hæmoglobinuric fever of man and the hæmoglobinuric fevers of cattle are most striking. To explain the fact that as yet no babesia has been found in cases of blackwater fever, I might suggest that either the amœboid forms of the parasite have been mistaken for the early forms of the subtertian parasite, or that the parasite has escaped observation on account of diminutive size or anatomical habitat, or because it is not usually found in the peripheral blood.

Edington claims to have shown that when cattle, natives of the endemic regions of Texas fever, are inoculated with rinderpest, they develop hæmoglobinuria, and the other symptoms of Texas fever, from which disease they might be supposed to be immune. The blood of immune cattle in Texas fever regions, we know, contains, in small number, the babesia. Edington's experiments show that the supervention of a second infection, rinderpest, determines the multiplication of the latent babesia, and the explosion of the characteristic babesia symptoms. May this not be in strict analogy with what happens in blackwater fever? The infection of blackwater fever may remain latent for considerable

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periods, until provoked into activity by some special agency, as cold, shock, quinine, or some additional infection, *e.g.*, malaria.

Manifestly, the ætiology of blackwater fever is not yet settled, and it is wise to preserve an open mind on this important subject.

Symptoms.—*Incubation.*—We know nothing definite as to the incubation period of blackwater fever. Scott, in British Central Africa, noticed that the attack usually occurred about eight days after exposure in certain low-lying districts. That the disease may remain in abeyance for a considerable time is proved by the facts that recurrences after long intervals—months—are very common, in fact the rule; and that in some cases the first attack may manifest itself in Europe several months after the patient has left the endemic regions. I have recently met with a case in England, in which a severe attack, followed by a still more severe and prolonged relapse, was the first manifestation of a blackwater fever infection which must have been acquired at least nine and a half months previously—the time that had elapsed since the patient left Africa.

The onset of blackwater fever is usually sudden. A slight or, more generally, a very severe rigor is followed by intermitting, or remitting, or irregular fever, with marked bilious symptoms. Earlier or later in the attack, usually during rigor, the patient becomes conscious of aching, perhaps severe pain, in the loins, in the region of the liver and spleen, and over the bladder; in exceptional instances these local pains are absent. In consequence of a somewhat urgent desire he passes water, when he is astonished to see that his urine has become very dark in colour, perhaps malaga-coloured, or possibly almost black. The fever continues, though not necessarily very high. Very likely he suffers from epigastric pain and distress, bilious vomiting to an unusual extent, and, it may be, bilious diarrhœa; or he may be constipated. The pain in the loins and the liver-ache continue, and the urine becomes darker and darker. By-and-by the sufferer breaks

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into a profuse sweat and the fever gradually subsides. The urine, which hitherto may have been somewhat scanty, now flows more freely; and, after passing through various paling shades, from dark brown to sherry red, becomes once more natural in appearance. Coincidently with the appearance of the dark colour in the urine, or even before this has been remarked, the skin and scleræ rapidly acquire a deep saffron-yellow tint. This icteric condition persists and even deepens during the progress of the fever, continuing for several days to be a striking feature of the symptoms. When the fever subsides, the patient is conscious of a feeling of intense weakness, from which he recovers but slowly. Fever may recur next day, or for several days; or it may cease; or it may be remittent, or almost continued in type. The hæmoglobinuria may recur with each rise of temperature; or there may be only one or two outbursts; it may continue for an hour or two only; or it may persist off and on for several days or even weeks.

In the more severe forms of hæmoglobinuric fever there is usually a very great amount of bilious vomiting, of intense epigastric distress, and of severe liver- and loin-ache. The urine may continue copious and very dark in colour; or, continuing hæmoglobinous, it may gradually get more and more scanty, acquiring a gummy consistence, a few drops only being passed at a time. Finally, it may be completely suppressed.

In severe cases death is the rule. It appears to be brought about in one of three or four ways. The fever may assume the typho-adynamic type; or suddenly-developed cerebral, hyperpyrexial or algide symptoms may supervene. In other cases the symptoms may be like those consequent on sudden and profuse hæmorrhage — jactitation, sweating, sighing, syncope. Or it may be that suppression of urine, persisting for several days, terminates, as cases of suppression usually do, in sudden syncope or convulsions and coma. Or, more rarely, nephritis may ensue and the patient die from uræmic trouble three or four weeks after all signs of hæmoglobinuria and fever have disappeared.

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Recently I saw in London a case in which the fatal issue appeared to have been brought about by persistent hiccough—always a bad sign—hepatitis, and vomiting of blood.

The urine.—If the characteristic dark brown, generally acid, urine of a hæmoglobinuric case be stood for some time in a urine glass, it will separate into two well-marked layers: an upper of a clear though very dark port-wine tint, and a lower—perhaps amounting to one-half or one-third of the entire bulk—of a somewhat brownish grey colour, and consisting of a sediment in which an enormous number of hyaline and hæmoglobin tube casts are to be found, together with a large quantity of brownish granular material. Epithelium is also met with. Blood corpuscles may be entirely absent, or very few in number. With the hæmoglobin there is also an escape of the serum-globulin of the blood, for the urine, in many cases, turns almost solid on boiling; the coagulum so formed carries down with it as it subsides the dissolved and suspended hæmoglobin, leaving a pale yellow supernatant urine. For some days after the urine has regained a normal appearance it will still contain albumin, though in gradually diminishing amount. Spectroscopic examination gives the characteristic bands of hæmoglobin, sometimes those of methæmoglobin.

Mortality.—This varies greatly in different epidemics, in the same and in different places, and even under the same treatment. Some cases are so mild and transient, amounting, perhaps, to a single emission of hæmoglobinous urine, with little or no fever, that they are unattended with risk; on the other hand, a practitioner may encounter a run of severe cases in which nearly all die. Some old residents in Africa have passed through ten or more attacks with impunity. Taking one with the other, the case mortality in blackwater fever may be put down at about twenty-five per cent.

Post-mortem appearances.—*The kidneys.*—If the kidneys of a fatal case are examined at an early stage of the disease, they are seen to be

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enlarged and congested, the tubules blocked with hæmoglobin infarcts, the cells laden with yellow pigment grains, and the capillaries most probably with a certain amount of malarial pigment. If the case survive for three or four weeks and then die of uræmia, the appearances are those of large white kidney.

The spleen is enlarged, congested, and usually contains malarial pigment.

The liver is enlarged, soft, of a dark yellow colour. Microscopically it reveals evidence of cloudy swelling with a large amount of hæmosiderin in the liver cells. Hæmozoin may or may not be present.

Diagnosis. — The diseases with which blackwater fever might be confounded are — 1, Paroxysmal hæmoglobinuria; 2, bilious remittent malaria; 3, yellow fever; 4, icterus gravis. If it be borne in mind that rigor, hæmoglobinuria, pyrexia, are all in evidence at the outset in blackwater fever, and also that blackwater fever is acquired only in certain countries, an error in diagnosis is improbable.

As regards paroxysmal hæmoglobinuria occurring in the tropics, a diagnosis might be impossible. Both diseases have the same symptoms. Paroxysmal hæmoglobinuria, as a rule, is of a milder type. In bilious remittent malaria an examination of the urine will suffice to exclude one of the characteristics of blackwater fever, namely, the presence of hæmoglobin. Moreover, the malaria parasite will be present in the blood throughout the fever until quinine has been administered. In yellow fever, the initial rigor is rarely severe, the appearance of icterus is a comparatively late event, the spleen and liver are not usually enlarged, the urine is albuminous, and if blood be present the erythrocytes are abundant. The same remarks apply to icterus gravis.

Treatment.—Having regard to the frequency with which hæmoglobinuric fever concurs with malarial infection, and the well-established fact that quinine may precipitate or determine a hæmoglobinuric attack, the question of the administration of that drug in hæmoglobinuria becomes an important point. Some

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practitioners of experience recommend the exhibition of the drug in heroic doses, giving it every two hours in divided doses to the extent of 120 grains a day; this they keep up till convalescence is established. On the other hand, hæmoglobinuria may come on while the patient is cinchonised. The Plehns, Koch, and others, after trying quinine in these cases, and carefully comparing the results of treatment both with and without quinine, abandoned its use. So long as the hæmoglobinuria continued they treated the case symptomatically, cautiously resuming the specific if the case merged into and concluded as a simple intermittent. There can be no doubt that in large doses quinine exercises a certain amount of destructive action on the blood corpuscles, rendering their hæmoglobin unstable. When, therefore, its toxic influence is superadded to that of the specific cause of the hæmoglobinuric fever, it may be that it supplies the little that is required to determine an extensive liberation of hæmoglobin, which, had the quinine been withheld, might not have taken place. Bastianelli lays down the following sensible rules as to the use of quinine in hæmoglobinuric fever:—(*a*) If hæmoglobinuria occurs during a malarial paroxysm and parasites are found in the blood, quinine should be given. (*b*) If parasites are not found in the blood, quinine should not be given. (*c*) If quinine has been already given before the hæmoglobinuria has appeared and no parasites are found, its use should be suspended; but if parasites persist it should be continued.

Recommendations.—Patients who are suffering from or are threatened with hæmoglobinuria, or who have had this disease before, on the slightest indication of fever should go to bed at once, keep their skins warm and scrupulously protected from draughts, and take plenty of warm fluid; if parasites are present in the blood, moderate doses—five grains—of quinine every three or four hours (intramuscularly by preference), and a moderate dose of calomel should be given.

When the urine tends to be suppressed, diuretics must not be given with the idea of stimulating the kidneys. In these circumstances hot fomentations

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should be applied to the loins, plenty of bland diluents administered, and an exclusive milk diet ordered until all albumin has disappeared from the urine. When, owing to persistent vomiting, fluid cannot be retained by the stomach, enemata of physiological salt solution (much less irritating to the bowel, and thus far more likely to be retained than plain water) should be administered repeatedly. If these are not retained, the salt solution (a teaspoonful to the pint of sterilised water), sterilised, may be slowly introduced into the subcutaneous connective tissue of the flank by means of a hollow needle attached by a rubber tube to some improvised reservoir placed one or two feet above the level of the patient. The water is rapidly absorbed, and cannot fail to be useful in washing out the hæmoglobin infarcts which plug the renal tubules and bring about, or at all events contribute to, suppression of urine. Marked restlessness may require minute doses of morphia ($\frac{1}{10}$ grain); but this drug, of great use at times, must be employed with caution. This is the only rational and safe systematic treatment of hæmoglobinuric fever. Antipyretics, as antipyrin and phenacetin, are dangerous.

Sternberg's mixture of bichloride of mercury and sodium bicarbonate has come into favour lately, especially in Central Africa.

Calomel in large doses—20 to 30 grains—is a favourite remedy with some for hæmoglobinuric fever. It has been systematically used in Africa in these cases. I have heard of its being given there by the teaspoonful. I know of cases which recovered perfectly without a grain of calomel or of quinine. Severe stomatitis may arise from the former; it should therefore be employed with great caution, and in reasonable dose.

Quennec has advocated the administration of small doses of *chloroform* in hæmoglobinuric fever. His formula is chloroform 4 grammes, powdered gum q.s., sweetened water 250 grammes: of this a tablespoonful is given every ten minutes until a certain degree of chloroform intoxication is produced. Thereafter the effect is kept up by enemas of chloral. In twenty-two successive cases he had no death.

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Tannic acid is another drug which enjoys a certain reputation in the treatment of malarial fevers which have resisted quinine, and also in hæmoglobinuric fever. It is given, well diluted, in fifteen-grain doses every two hours for four or five times, the dosing being repeated on the third and sixth days to the extent of two doses each day.

Salicylate of soda, boracic acid, chloride of calcium, potash, preparations of Beereana, are used by some medical men in West Africa at the present time, and, it is said, as of many other drugs, with good results.

Transfusion of blood has been successfully practised in high degrees of anæmia in some of these cases. *Oxygen* inhalations are indicated, but are rarely practicable.

Nursing is a most important element in the management of these cases. If the stomach will retain food this should be given in a bland and fluid form, but there should be no attempt to force feeding, especially with rich and indigestible viands. One precaution against syncope must be sedulously enforced: the patient must not be allowed to sit up, much less to get out of bed, until food has been retained and assimilated and the risk of sudden death from syncope has passed.

If possible, the subject of a hæmoglobinuric attack should quit the endemic area, and never return to it, or to any malarial locality; a severe attack, or a second attack, implying as they would special liability, should be regarded as imperative indications to this effect.

Prophylaxis.—All depressing and predisposing causes must be carefully avoided, more especially chill, fatigue and malaria, and also irregular dosing with quinine. In blackwater regions those who are the subjects of malarial infection should take quinine systematically, never irregularly, and should be especially careful to continue its use, in the accustomed doses and at the accustomed intervals, for at least six months after arrival in Europe. Most of the cases of blackwater I have seen in this country were, I believe, attributable to neglect of

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this precaution and to a big dose of quinine taken for a relapse of a malarial infection supposed to have died out. Those who have had blackwater should gradually habituate themselves to quinine, beginning with minute doses slowly increased to five grains, which dose they should take daily while under the endemic influences, and at least for six months afterwards.

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CHAPTER XV

SPOTTED FEVER OF THE ROCKY MOUNTAINS

For some thirty years a peculiar disease variously named "spotted fever," "blue disease," "black fever," has been recognised as endemic in limited districts of Montana and Idaho, United States of America. It was first described by Maxey, in 1899, as a distinct disease, and, in the spring of 1902, it was investigated by Wilson and Chowning, who attributed it to the presence in the blood of a parasite akin to the babesia of Texas cattle fever. Their results were endorsed by Wesbrook, Cobb and Anderson; but in May, 1904, Wardell Stiles failed to recognise the parasite, both in fresh preparations of the blood and in the preparations of previous investigators.

The disease has been reported for several of the Western States of the American Union—Idaho, Montana, Wyoming, Utah, Nevada, Oregon, and Washington State. It is believed to occur also in the territory of Alaska. It is found principally in valleys and near the foot-hills of mountains in sharply-defined and limited areas, and is confined to the spring months, the greatest number of cases occurring between March and July. It attacks any age, either sex, and is not directly contagious.

Symptoms.—A short period of malaise is followed by chills, which are repeated with diminishing severity at irregular intervals throughout the attack. By the second day the temperature has risen to 103° or 104° F., and by the fifth day to 105° or 107° F. A typhoid-like condition with low muttering delirium and semi-consciousness is rapidly developed. If the patient is to recover, the temperature begins to fall about the end of the second week, fever subsiding usually by lysis.

About from the fourth to the seventh day, an

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eruption appears on the wrists, ankles, or back, extending rapidly to the trunk, scalp, hands, and feet. At first it consists of minute rose-coloured spots; these soon assume a petechial character and, spreading, tend to become confluent, especially on the more dependent parts of the body and limbs. In other instances the spots remain discrete, brownish or purplish in colour, giving to the surface of the body a speckled appearance. A certain amount of icteric tinting of skin and scleræ is also present. During the third week desquamation sets in, the eruption fading as fever subsides. In some cases the skin of the elbows, fingers, toes, lobes of the ears, etc. becomes gangrenous.

Constipation is usual. The liver is slightly enlarged, the spleen markedly enlarged and tender. The scanty, high-coloured urine may contain albumin and casts. Early, in all severe cases, there is œdema of the face and limbs. Nausea and vomiting set in about the beginning of the second week, and persist in fatal cases. Respiration is rapid. A slight catarrhal condition of the respiratory tract is present throughout; the pulse loses in volume as it increases in frequency. There appears to be but slight diminution in the blood count, and only a feeble leucocytosis—12,000 to 13,000; the hæmoglobin is slightly diminished.

Pathology.—*Post-mortem*, in addition to the foregoing skin lesions, there is marked hypostatic congestion of the lungs, subserous petechiæ, softened myocardium, enlarged and softened spleen, fatty degeneration of the hepatic cells, and congestion of the cortex of the kidneys.

Ætiology.—Wilson and Chowning stated that they found in the red blood corpuscles an unpigmented hæmoprotozoon, rather larger than, but closely resembling, *Babesia bigemina*. In peripheral blood about 1 in every 500 corpuscles contained the parasite; in blood from the liver, spleen, kidneys, and lungs about every fifth corpuscle was infected, many of the invaded corpuscles being included in phagocytes.

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These observers describe two phases of the parasite—a small and large—with transition forms. The small parasites, 1·5 to 2μ by 1μ, are ovoid in form, non-amœbic, and usually occur singly; in about 1 in every 10 infected corpuscles the invasion was double, the twin parasites being generally arranged so that their smaller ends approximated without quite touching each other. The larger forms are always single; usually ovoid in shape, they measured from 2 to 3μ by 3 to 5μ. In freshly-drawn blood the larger forms are actively amœboid, pushing out and retracting pseudopodia. Besides these, minute coccus-like bodies are present in the plasma, resembling in

Fig. 52.—Dermacentor reticulatus, distended; female.

size and staining properties the smaller type of intra-corpuscular parasites. All forms stain but imperfectly with methylene blue, the stain being most intense at the smaller end of the organisms.

Wilson and Chowning suggested that this parasite is proper to the burrowing squirrel or common grey spermophile (*Citellus columbianus*) of the districts in which it occurs, and that it is transmitted by the bite of a tick (*Dermacentor reticulatus*), the geographical and seasonal limitations of the disease apparently favouring such an idea. Although all their patients, eleven in number, had been bitten by ticks—three of them only a few days before the appearance of the disease—these observers have given so far no experimental proofs of the truth of their hypothesis. Such proofs ought not to be difficult to

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obtain, seeing that they found that rabbits are susceptible to direct inoculation by infected blood.*

Many local observers consider Spotted Fever to be typhus exanthematicus, and Sambon, in a recent article, takes up this position both on clinical and epidemiological grounds, pointing out that typhus may not be immediately communicable as generally believed, but that it is probably transmitted by insect intermediaries. With regard to Wilson's and Chowning's observations, he remarks that about the same time Gotschlich claimed to have found a Babesia in the blood of typhus patients in Egypt, and considers the protozoan nature of that disease as very probable. The tick medium he also regards as not improbable, such a mode of transmission in the Western American States being supported by the analogy of relapsing fever, which is conveyed by ticks in Africa, and by the common bed-bug or some other blood-sucking insect in Europe.

Mortality.—There is a striking difference in the mortality of the disease between the States of Idaho and Montana. In Idaho it is about 2·5 per cent., in Montana from 70 to 80 per cent., and in some years even 90 per cent.

Treatment and prophylaxis.—In the absence of a specific remedy, treatment must be conducted on general principles, having regard to the natural history and nature of the disease. Attempts at prophylaxis might be based on the above-described hypothetical method of transmission of the disease.

* Quite recently Ricketts has given experimental support to the theory of tick transmission.

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CHAPTER XVI

DENGUE

Definition.—Dengue—derived, according to Hirsch, from the Spanish equivalent of "dandy"—is the name applied to a specific and highly infectious fever peculiar to warm climates. It occurs usually in widespread epidemics. Once introduced into a community it extends with great rapidity, affecting a large proportion of the inhabitants. In these respects it resembles influenza, a disease with which it has been confounded. Dengue, however, differs from influenza in many respects, chiefly in being attended with a well-marked rubeoloid eruption and peculiarly severe rheumatic-like pains in the joints and limbs, and in not being accompanied or followed by pulmonary and other serious complications.

Geographical distribution and mode of spread.—Most parts of the tropical world have been visited at one time or another by dengue. From a study of the dates of the various epidemics, it would seem that there is a tendency for it to assume pandemic characters about once in every twenty years. Perhaps of all places in the world it is most frequently met with in the West Indies.

Recently dengue has appeared in Syria, Asia Minor, on the Ægean shores of Greece and Turkey, and in North Queensland, Australia. Early in the last century it was seen in America, as far north as Charleston and Philadelphia in the United States, and as far south as São Paulo in the Brazils.

Like other infectious diseases, dengue tends to advance along trade routes and lines of communication. Thus, starting from Zanzibar, the epidemic of 1870–73 first reached Aden. Thence it travelled to Suez on the one side and to India on the other. Passing to Singapore, it followed the trade routes to

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Cochin China and China, spreading at the same time to the islands of the Eastern Archipelago. From India it was carried by the coolie ships to Mauritius and Réunion in 1873.

An epidemic which I witnessed in Amoy (1872) illustrated very well a characteristic feature of dengue epidemics—namely, the peculiar suddenness of their rise and extension, and the general prevalence of the disease in an affected community. I am under the mark when I say that in this particular epidemic quite 75 per cent. of natives and foreigners were attacked within a very few weeks. All ages and occupations, both sexes, and people in every condition of life, were alike subject to it. About the first week in August I heard that a peculiar disease had appeared in the town; by the end of the second week the cases were numerous, whole families being prostrated at a time. A week later the cases were still more numerous, and by the end of the month so general was the disease that the business of the town was seriously interfered with. By the end of the following month —that is to say, in about eight weeks from the first appearance of the epidemic—all the susceptible apparently had passed through it, and, so far as Amoy residents were concerned, the disease was at an end, cases occurring for a few weeks longer only in visitors from unaffected districts. This course seems to be fairly typical of all dengue epidemics.

Ætiology.—*Germ.*—Various bacteria have been described. Graham describes an intracorpuscular amœba, resembling *Babesia bigemina*, which he states he found in great profusion in the blood of dengue patients in Beyrout, Syria. He maintains that his experiments tend to show that, like yellow fever, dengue is communicated by a mosquito, *Culex fatigans*. Bancroft, who considers that the germ is ultramicroscopic, has advanced the same view in Australia in favour of *Stegomyia fasciata*. Recent experiments by Ashburn and Craig, made under favourable conditions, seem to show that the germ of dengue resides in the liquor sanguinis, that it is ultramicroscopic, that injected into non-immunes it

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gives rise to typical dengue, that under natural conditions it is transmitted by *Culex fatigans*, that the incubation period of the experimental disease is from three to fourteen days, and that it is not contagious in the ordinary sense of that word.

Influences of meteorological conditions.—When dengue spreads beyond its ordinary tropical limits, as, for example, in the epidemics of Philadelphia and Asia Minor, the extension occurs only during the hottest part of the year—in the late summer and early autumn. Hitherto, such epidemics have been arrested on the approach of winter. Even when occurring within the tropics, dengue prevails principally, though not exclusively, during the hottest part of the year. High temperatures, therefore, seem to be one of the conditions it demands.

Epidemics occur indifferently during the dry or the rainy seasons, the hygrometric condition of the atmosphere being without manifest influence.

Usually a coast disease.—It would appear that dengue, like yellow fever, prefers the coast line and the deltas and valleys of great rivers to the interior of continents. There are many exceptions to this rule; in 1870–73 it spread all over India. The distribution and concentration of population on the sea-board and along rivers, and the freedom of communication between communities so located, probably determine this preference.

As a rule, elevated places enjoy a relative immunity; if the disease is introduced into such localities, it does not spread. To this, again, there are exceptions, for the Syrian epidemic referred to prevailed in certain spots 4,000 to 5,000 feet above the sea.

The **incubation period** seems to be somewhat variable. It is certainly not a long one. I have seen a case in which it could not have exceeded twenty-four hours. Some observers place it at five and even seven days; this, I feel sure, is an over-estimate. One to three days seems to be near the truth.

Symptoms.—*Initial fever and eruption.*—An attack of dengue may be preceded for a few hours by a feeling of malaise or, perhaps, by painful rheumatic-

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like twinges in a limb, toe, finger, or joint. Usually it sets in quite suddenly. A patient, describing his experience, said that in the morning he got up feeling quite well, but before he could complete his dressing he was so prostrated by pain and fever that further exertion was impossible, and he had to crawl back to bed again. Similar stories, illustrative of the sudden incidence of the symptoms, circulate during every epidemic of dengue. Sometimes the fever is ushered in by a feeling of chilliness or even by a smart rigor; sometimes a deep flushing of the face is the first sign of the disease.

However introduced, fever rapidly increases. The head and eyeballs ache excessively, and some limb or joint, or even the whole body, is racked with peculiar stiff, rheumatic-like pains, which, as the patient soon discovers, are very much aggravated by movement. The loins are the seat of great discomfort, amounting in some cases to actual pain; the face—particularly the lower part of the forehead, round the eyes, and over the malar bones—becomes suffused a deep purple; and often the skin over part or the whole of the body, and all visible mucous surfaces are more or less flushed, that of the mouth and throat being sore from congestion and perhaps from small superficial erosions. The eyes are usually much injected; very often the whole face is bloated and swollen. This congested erythematous state of the skin constitutes the so-called initial eruption.

These symptoms becoming in severe cases rapidly intensified, the patient, in a few hours, is completely prostrated. His pulse has risen to 120 or over; his temperature to 103°, in some cases to 105°, or even to 106°. He is unable to move owing to the intense headache, the severe pain in limbs and loins, and the profound sense of febrile prostration. From time to time the skin may be moistened by an abortive perspiration, but for the most part it is hot and dry. Gastric oppression is apt to be urgent, and vomiting may occur. Gradually the tongue acquires a moist, creamy fur which, as the fever progresses, tends to become dry and yellow.

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Defervescence.—In this condition the patient may continue from one to three or four days, the fever declining somewhat after the first day. In the vast majority of cases this, the first and most acute stage, is abruptly terminated about the end of the second day by crisis of diaphoresis, diarrhœa, diuresis, or epistaxis. When epistaxis occurs the relief to the headache is great and immediate. On the occurrence of crisis the erythematous condition of the skin, if it has not already disappeared, rapidly subsides. In a proportion of cases, and particularly in certain epidemics, crisis does not occur, the fever slowly declining during a period of three or four days. Thus the urgent symptoms abate, and the patient rapidly, or more slowly, passes from what, in many cases, may be described as the agony of the first stage to the comparative calm and comfort of the second.

The interval.—When the second stage is established and the thermometer has sunk to normal, the patient is sufficiently well to leave his bed and even to attend to business. An occasional twinge in leg, arm, or finger, or a tenderness of the soles of the feet, and perhaps giddiness in walking, may remind him of what he has gone through and warn him that he is not quite well yet. But the tongue cleans, and the appetite and sense of well-being return to some extent.

Terminal fever and eruption.—This state of comparatively good health continues to the fourth, fifth, sixth, or even to the seventh day counting from the commencement of the illness. Then there is generally a return of fever, slight in most cases, more severe in others. It is usually of very short duration—a few hours. Sometimes this secondary fever does not occur; probably it is often overlooked. With the recurrence of the fever an eruption of a rubeolar character appears. The pains likewise return, perhaps in more than their original severity. Though the fever subsides in a few hours, the eruption, at times very evanescent, may keep out for two or three days longer, to be followed very generally by an imperfect furfuraceous desquamation. It seldom

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happens that the fever or pains at this stage keep the patient in bed, although that is the best place for him if a comfortable and speedy convalescence is desired. Rarely, in this secondary fever, does the thermometer rise to 103°. The temperature falls rapidly to below normal on the setting in of diaphoresis, or diarrhœa, or of some form of crisis.

Characters of the eruption.—The terminal eruption of dengue possesses very definite characters. It is absent in a very few cases only; in many of those cases in which it is supposed to be absent, being slight, it is overlooked. As stated, the eruption is rubeolar in character. It usually commences on the palms and backs of the hands, extending for a short distance up the forearms. Its development is often associated with sensations of pricking and tingling. On the palms of the hand the spots are at first about the size of a small pea, circular, dusky red, and sometimes slightly elevated. The eruption quickly extends, and is best seen on the back, chest, upper arms, and thighs. In these situations it appears at first as isolated, slightly elevated, circular, reddish brown, rubeoloid spots, from one-eighth to one-half of an inch in diameter, thickly scattered over the surface, each spot being isolated and surrounded by sound skin. After a time the spots, enlarging, may coalesce in places; thus irregular red patches from one to three inches in diameter are formed. Or, perhaps, there is a general coalescence of spots, isolating here and there patches of sound skin; in this case the islands of sound skin give rise, at first sight, to the impression that they constitute the eruption—a pale eruption, as it were, on a scarlet ground. In a few instances the whole integument may be covered with one unbroken sheet of red. The rash is usually most profuse on the hands, wrists, elbows, and knees; in these situations it is generally coalescent, and there, too, it may be detected though absent elsewhere. The spots disappear on pressure, and never or rarely become petechial. They fade in the order in which they appear—first on the wrist and hands; then on the neck, face, thighs and body; last on the legs and feet.

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Desquamation.—Desquamation may go on for two or three weeks. In many it is trifling in amount; for the most part it is furfuraceous. Rarely does the epidermis peel off in flakes of any magnitude; never in the broad sheets seen after scarlatina. Often for a day or two desquamation is accompanied by intense pruritus.

Convalescence.—In some instances, and in some epidemics, the disease terminates with the fading of the eruption; appetite and strength gradually return, and the patient, after a few days of debility, feels quite well again.

The rheumatoid pains.—With most, their troubles do not end so soon. For days or weeks some muscle, tendon, or joint is the seat of the peculiar pains, which may become so severe as to send their victim back to bed again. Sometimes, three or four weeks after all apparent trace of the disease has vanished, a joint or a muscle will be suddenly disabled by an attack of this description. This may occur in patients who, during the acute stage, suffered little or no pain. A finger or toe, or a joint of a finger or of a toe, may alone suffer. Of all the joints, perhaps the knee is most frequently affected; but wrists or shoulders are often attacked, and their associated muscles may even undergo considerable atrophy from enforced disuse. The soles of the feet, too, and the tarsal articulations are favourite sites.

The pains of dengue, those occurring during the initial fever as well as those that may be regarded as sequelæ, are difficult to locate with precision; the joints or muscles affected may be percussed, pressed, or moved with impunity. Du Brun locates those associated with the knee in the thigh muscles, which, he says, are painful on deep pressure.

The pains are worst usually on getting out of bed in the morning, and on moving the affected part after it has been at rest for some time. They are relieved somewhat by rest and warmth. Passive movements are, as stated, not painful, but any resistance to the movement of the limb may cause acute suffering. When a muscle is affected the pain is accompanied by a sense of powerlessness

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Other complications and sequelæ.—Convalescence may be very much delayed by the persistence of these pains; also by anorexia, by general debility, mental depression, sleeplessness, evanescent feverish attacks, boils, urticarial, lichenoid and papular eruptions, and by troublesome pruritus. Among sequelæ and complications may be mentioned enlargement of the lymphatic glands (particularly the superficial cervical), orchitis, possibly endocarditis and pericarditis, hyperpyrexia, purpura, and hæmorrhages from the mouth, nose, bowel, and uterus. Miscarriage is rare. The urine sometimes contains a trace of albumin, but true nephritis does not occur.

Variability of epidemic type.—Judging from the published descriptions, there is considerable variety in the symptoms of this disease in different places and in different epidemics. Some authors mention swelling and redness of one or more joints as a common and prominent symptom; others refer to metastasis of the pains, enlargement of the submaxillary glands, orchitis, mental depression, hæmorrhages, and so forth, as being frequently present. However this may be, the essential symptoms in well-marked cases are the same practically everywhere, and in all epidemics; these are, suddenness of the rise of temperature, an initial stage of skin congestion, limb and joint pains, and a terminal rubeoloid eruption.

Relapses are not uncommon in dengue, and second and even third attacks during the same epidemic have been recorded. As a rule, however, susceptibility to the disease is exhausted by one attack. According to Hare, in the recent Australian epidemic the immunity acquired by an attack did not persist beyond one year.

Mortality.—In uncomplicated dengue the mortality may be said to be almost *nil* (0·1 per cent., Hare). In the case of very young children, convulsions and delirium may occur and cause anxiety; and in the aged and infirm, and in those suffering from chronic exhausting disease, an attack of dengue may prove a serious complication. Charles describes a pernicious form which, though rare, was very much

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dreaded in Calcutta. In these cases the lungs became œdematous, and the patient, growing drowsy and cyanotic, rapidly passed into a comatose condition with a tendency to hyperpyrexia, and died. Some writers state that the gravity of any given case is in direct proportion to the abundance of the eruption; others deny this.

In Europeans an attack of dengue very often leads to a condition of debility necessitating temporary change of climate, or even return to Europe. In both Europeans and natives the attendant lowering of the resistive powers predisposes to other and more dangerous diseases, such as malaria, dysentery, phthisis, and so forth; consequently dengue, otherwise a benign disease, may become a source of public danger. It is probable that it is in this indirect way that the general mortality is increased during a visitation of this disease, as has been observed in several epidemics.

Morbid anatomy.—On account of the low mortality, *post-mortem* records are few. Nogué, who observed two epidemics of dengue in Cochin China (1895–96), made four *post-mortem* examinations in this disease. In these, pulmonary and intracranial inflammation were the special features. The meningitis amounted to adhesions and sero-purulent infiltration of the pia mater.

Diagnosis.—Dengue must not be confounded with yellow fever, rötheln, scarlatina, measles, syphilitic roseola, influenza, cerebro-spinal meningitis, rheumatic and malarial fevers. A knowledge of the distinctive features of these diseases, and the fact that dengue is attended with a rash and with articular pains, and that it occurs in great and rapidly-spreading epidemics, should prevent any serious error in diagnosis.

Treatment.—Were it possible to secure perfect isolation for the individual during an epidemic of dengue, doubtless he would escape the disease. Even comparative isolation is attended with diminished liability. In Amoy, in the epidemic of 1872, those foreigners who lived in a more or less isolated suburban situation were very much less affected than

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were those who lived in the native town, or than those whose occupations threw them much into contact with the natives. But though this and similar facts point to the theoretical possibility of avoiding dengue during an epidemic, in the ordinary conditions of life in the tropics prophylactic measures for the mass are impracticable. Specially delicate individuals, particularly the subjects of tubercular or renal disease, should be isolated, or, better, should leave for a time the epidemic locality.

Like the allied fevers, dengue runs a definite course; therefore it is useless to attempt to cut it short. The patient should go to bed so soon as he feels ill, and he should keep his room till the terminal eruption has quite disappeared and he feels well again. Ten days is not too long to allow in severe attacks. As in influenza, light liquid diet, rest, and the avoidance of chill conduce powerfully to a speedy and sound convalescence. At the outset of the fever some saline diaphoretic mixture, with aconite, may be prescribed with advantage. If the pains be severe and the fever high, antipyrin, or phenacetin, or belladonna will give great relief. Cold applications to the head are comforting. If the temperature rises to 105° or over, cold sponging or the cold bath ought to be had recourse to. If the pains continue very distressing, a hypodermic injection of morphia will afford welcome relief and do no harm. Purgatives and emetics should be avoided unless pronounced constipation, or a history of surfeit, urgently demands their exhibition. The pain caused by the muscular movements entailed by the efficient action of purgatives more than counterbalances any advantage the latter might otherwise bring. Wine in the early stage is not advisable. Freshly made lemonade, or iced water, will be found acceptable drinks during the fever.

For the pains experienced during convalescence, rubbing with opium or belladonna liniment, gentle massage, electricity, salicylates, small doses of iodide of potassium and quinine have been advocated. Debility or anorexia indicates tonics such as quinine, strychnine, mineral acids, vegetable bitters, and change of air.

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CHAPTER XVII

JAPANESE RIVER FEVER (SHIMA MUSHI)

Definition.—An acute endemic disease running a definite course and attended with a considerable mortality. It is characterised by the presence on the skin of an initial eschar, followed by an ulcer, lymphatitis, fever, an exanthematous eruption, bronchitis, and conjunctivitis.

History.—This disease was first described by Palm in 1878, and subsequently, and more fully, by Baelz and Kawakami.

Geographical and seasonal distribution.—So far as known, shima mushi is confined to the banks of two rivers on the west side of the island of Nippon—the Shinanogawa and one of its tributaries, and the Omonagawa. Every spring these rivers inundate large tracts of country. Later in the year hemp is raised on strips of the inundated district. The crop is reaped in July and August, and it is solely among those engaged in harvesting and handling this that the disease occurs. It is not communicable by the sick to the healthy. Although transportable in the hemp to a very slight extent, it is only in limited spots here and there in the endemic districts that the virus originates.

Ætiology.—The Japanese attribute this disease to the bite of an acarus (locally called *aka mushi*—red insect) resembling the *Leptus autumnalis* of Europe. Baelz rejects this idea, but does not explain how otherwise the virus is introduced. Men, women, and children are equally susceptible. One attack does not confer immunity, although it may render subsequent attacks less severe. As yet the virus of the disease, which doubtless enters in the first instance at the site of the primary eschar, has not been discovered.

Symptoms.—After an incubation period of from four to seven days the disease usually begins with

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malaise, frontal and temporal headache, anorexia, chills alternating with flushes of heat, and prostration. Presently the patient becomes conscious of pain and tenderness in the lymphatic glands of the groin, armpit, or neck. On inspecting the skin of the corresponding lymphatic area there is discovered—usually about the genitals or armpits—a small (2 to 4 mm.) round, dark, tough, firmly adherent eschar surrounded by a painless livid red areola of superficial congestion. Occasionally two or three such eschars are discovered. Although a line of tenderness may be traced from the sore to the swollen, hard, and sensitive glands, no well-defined cord of lymphatitis can be made out. The superficial lymphatic glands of the rest of the body, especially those on the opposite side corresponding to the glands primarily affected, are also, but more slightly, enlarged.

Fever of a more or less continued type now sets in, the thermometer mounting in the course of five or six days to 40° or 41° Cent. The conjunctivæ become injected, and the eyes somewhat prominent; at the same time a considerable bronchitis gives rise to harassing cough. The pulse is full and strong, ranging rather low—80 to 100—for the degree of fever present. The spleen is moderately but distinctly enlarged, and there is marked constipation.

About the sixth or seventh day an eruption of large dark red papules appears on the face, tending to become confluent on the cheeks. It then extends to the forearms, legs, and trunk, being less pronounced on the upper arms, thighs, neck, and palate. Simultaneously with the papules a minute lichenous eruption breaks out on the forearms and trunk. This lasts usually from four to seven days; if but slightly marked it may fade in twenty-four hours.

The patients during the height of the fever are flushed, and at night, it may be, delirious. They complain incessantly, probably on account of a general hyperæsthesia of skin and muscles. Deafness is also a feature.

As the disease advances, the symptoms become more urgent; the conjunctivitis is intensified, the

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cough becomes incessant, the tongue dries, the lips crack and bleed, and there may be from time to time profuse perspiration. By the end of the second week —sooner or later according to the severity of the case—the fever begins to remit, the tongue to clean, and, after a few days, temperature falls to normal, and the patient speedily convalesces. Diarrhœa or diuresis may occur during the decline of the fever. The circular, sharp-edged, deep ulcer left after the separation of the primary eschar—an event which usually takes place during the second week—now begins to heal, and the enlargement of the glands gradually to subside.

Such is the course of a moderately severe case. In some instances, however, the constitutional disturbance is very slight, although the primary eschar may be well marked and perhaps extensive. On the other hand, the fever may be much more violent, and complications such as parotitis, melæna, coma, mania, cardiac failure, or œdema of the lungs may end in death. Similarly, the duration of the disease varies according to severity from one to four weeks, three weeks being about the average.

Pregnant women contracting shima mushi mostly abort and die.

The **mortality** in those attacked is approximately about 15 per cent.

Pathological anatomy.— Beyond evidences of bronchial catarrh, hypostatic pneumonia, enlarged spleen, perisplenitis, patchy reddening of the intestine near the ileo-cæcal valve, injection of the peritoneum, and slight enlargement of the mesenteric and superficial lymphatic glands, no noteworthy lesions have been described.

Treatment.— On the supposition that the disease is introduced by an insect, or through a wound of some sort, care should be exercised by those engaged in hemp culture in the endemic district to protect and keep clean the skin, especially that about the genitals and armpits. There is no specific remedy for the disease; treatment must therefore be conducted on general principles.

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CHAPTER XVIII

PLAGUE

Definition.—Plague is a specific, inoculable, and otherwise communicable epidemic disease common to man and many of the lower animals. It is characterised by fever, adenitis, a rapid course, a very high mortality, and the presence of a specific bacterium, *Bacillus pestis*, in the lymphatic glands, viscera and blood. In a large proportion of cases buboes form in the groins, armpits, or neck.

Geographical distribution. — Though not necessarily confined to warm climates, in modern times plague, like leprosy, has practically become so. The hygienic conditions which advancing civilisation has brought in its train have forced back these two diseases from Europe, where at one time they were even more prevalent than they are in their present tropical and subtropical haunts. Plague and leprosy are typical examples of that large group of acute and chronic germ diseases whose spread depends on social and hygienic, rather than on climatic conditions, and more especially on the verminous accompaniments of filth and overcrowding: conditions which nowadays are found, to an extent and an intensity sufficient to ensure the endemic prevalence or epidemic extension of these diseases, for the most part, only in warm countries.

It is difficult to say what the *pestis* of the ancients may have been. Probably in many instances it was bubonic plague; doubtless the term was sometimes applied to other epidemic sicknesses attended with a large mortality.

The descriptions which have come down to us of these old-world epidemics are too vague for recognition. According to Hirsch, the first recognisable description of what is now understood by plague

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refers to its occurrence in Libya, Egypt, and Syria about the end of the third and the beginning of the second century before the Christian era. The next authentic account, and the first as regards Europe, refers to the great epidemic known as the plague of Justinian, which, in A.D. 542, starting from Egypt, spread to Europe and all over the Roman Empire, and which, lasting for fifty or sixty years, wrought the most frightful devastation wherever it reached, depopulating the towns and turning the country into a desert. From that time until 1841, when plague appeared for the last time in Constantinople, it recurred again and again in different parts of Europe, though latterly only in the south-eastern parts of the continent and in areas becoming gradually more circumscribed. In 1878–79 a small epidemic, which speedily died out, broke out in the Russian province of Astrakhan. With the latter exception and the limited epidemic at Oporto in 1899 and at Glasgow in 1901, and a few isolated and mostly imported cases at the large seaports, Europe has long enjoyed exemption from this worst of epidemic diseases. The plague, as a widespread epidemic, visited England for the last time in 1664–79, when, in 1664–65, upwards of 70,000 of the 460,000 inhabitants of the London of that day perished.

Egypt, in former times a favourite haunt of the disease, until 1899 had been exempt since 1844, although several epidemics have since the latter date occurred in its neighbourhood—in Tripoli (Benghasi) in 1856, in 1859, and in 1874; and on the Red Sea coast of Arabia (Assir) from 1853 to the present time. It is now known to be endemic in Uganda and in the hinterland of German East Africa.

Many epidemics have occurred in Mesopotamia (last in 1892), in Turkestan (last in 1892), in India, in China, and in Mongolia. In India there were several outbreaks during the nineteenth century, but, with the exception of the current epidemic, they were of a localised rather than of a general character. One, beginning in Cutch in 1815, spread to Scinde and Gujerat, and continued

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till 1821. Epidemics have also occurred in Kumaon and Gharval on the southern slopes of the Himalayas in 1824, 1834–37, 1846–53, 1876, and 1884; also at Hansi in Delhi, 1828–29. In 1836 it appeared at Bareilly, Rohilcund, and at Pali in Rajputana, spreading to Jodhpore and to Marwar, and continuing till 1838. Probably plague is always present in some part of India, especially among the rude hill-peoples.

It is now known that plague has been endemic in the south-west of China, in the province of Yunnan, for many years. It is probable that the present extension of plague had its origin in that part of China. There it was seen by Rocher and others in 1878 and afterwards. It was particularly active in 1871–73, after the great Mahommedan rebellion. From Yunnan, probably following the trade route, it spread to Pakhoi on the Gulf of Tonquin, a severe epidemic occurring in 1883 in that and in neighbouring towns. In 1894 it had extended to Canton, where it killed, it is estimated, 60,000 in a population of 1,500,000 (?). Later in the spring of the same year it broke out in the English colony of Hong Kong, subsequently spreading to Macao, Swatow, Amoy, Foochow, Formosa, and probably to many other places in the southern provinces of the Chinese empire, where, in one place after another, considering the wretched hygienic conditions and the poverty of the inhabitants, it is safe to prophesy that plague will continue epidemic for many years to come. Japan and the Philippines were both infected from China.

Having probably been imported from Hong Kong it appeared in 1896 at Bombay, and subsequently as a great epidemic spread to Calcutta, and to many other parts of India where it still prevails. Indian official returns give the total plague mortality from the current epidemic up to December, 1905, as 4,097,764.

Soon after its appearance in India, plague became extensively epidemic in Mauritius, where it still prevails at certain seasons. Madagascar, Delagoa Bay,

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Cape Town, Port Elizabeth in Cape Colony, and Durban; also Sydney and Brisbane in Australia, and Alexandria in Egypt, have all been invaded.

Until its recent appearance in Brazil, the Argentine and other South American countries, in San Francisco and Mexico, plague had never invaded the western hemisphere.

Ætiology.—*The micro-organism.*—The proofs are now complete that the specific cause of plague is the cocco-bacillus which was discovered first by Kitasato

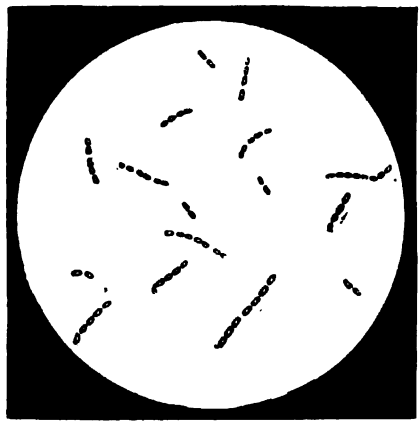

Fig. 53.—Bacillus of plague in chains showing polar staining. From a young culture in bouillon. (× 1000.) (*Muir and Ritchie.*)

and afterwards, independently, by Yersin during the Hong Kong epidemic in 1894. This microbe occurs in great profusion in the characteristic buboes—generally in pure culture, although towards the later stages it is often associated with the streptococci and staphylococci of suppuration. It is also present, and in great abundance, in the spleen, intestines, lungs, kidneys, liver, and other viscera, and also, though in smaller numbers, in the blood. In the pneumonic type of the disease it is present in the sputum in enormous numbers. It occurs also in the urine and fæces; in the latter, though detectable by inoculation

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and by cultivation, the bacillus may be hard to find by direct observation. Towards the termination of rapidly fatal cases it may become so abundant in the blood as to be readily observed there with the microscope.

The plague bacterium (Fig. 53), as seen in smearings or scrapings from the pulp of the buboes, or from any of the inflamed lymphatic glands, or from the viscera, is a short, thick cocco-bacillus (1·5 to 1·5μ and ·5 to ·7μ) with rounded ends, very like that of chicken cholera. Gordon says it has one terminal flagellum. A capsule, according to the same observer, or the appearance of a capsule, can generally be made out, especially in those bacilli which are present in the blood. The bacillus is readily stained by aniline dyes, the extremities taking on a deeper colour than the interpolar part. It is usually decolorised by Gram.

Culture characters.—When sown on blood serum and kept at body temperature, in from twenty-four to forty-eight hours an abundant moist, yellowish-grey growth is formed without liquefaction of the culture medium. On agar, but better on glycerine agar, the growths have a greyish-white appearance. In agar plate cultures they show a bluish translucence, the individual colonies being circular, with slightly irregular contours and a moist surface. Young colonies are glass-like, but older colonies are thick at the centre and more opaque. Stab cultures show after one or two days a fine dust-like line of growth. According to Yersin, when sown on gelatine the bacillus gives rise to white transparent colonies which, when examined in reflected light, present iridescent borders. In bouillon the cultures present a characteristic appearance; the liquid remains clear, whilst a granular deposit takes place on the sides and bottom of the tube. Examined with the microscope, these various cultures show chains of a short bacillus, presenting here and there large bulbous swellings. In gelatine the bacilli sometimes form fine threads, sometimes thick bundles made up of many laterally agglomerated bacteria. The bacillus does not form spores.

The most favourable temperature for culture is from 36° Cent. to 39° Cent.

Intensification and attenuation of virus.—There can be no question that, both by artificial means and in a natural way, the virulence of the bacillus of plague is susceptible of modification.

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It has been remarked in Russia, in Persia, and in Calcutta that certain outbreaks of plague were preceded by a sporadic, or epidemic febrile, sometimes afebrile, affection, in the course of which the lymphatic glands became enlarged and perhaps suppurated. Cases of this nature, in which a bacteriological examination proved that a coccobacillus was present in the blood and enlarged glands, are recorded by Drs. Cobb and Simpson. It is further known that in some instances the virulence and case mortality of a plague epidemic show a tendency to decrease, the early cases being the most frequently and most rapidly fatal. Recent observations in India have brought to light a form of chronic plague in rats, in which the specific bacterium, without seriously affecting the health of the animal, remains latent for long periods in abscesses in connection with spleen, liver, or abdominal lymphatics. Although thus latent, it is potentially virulent, proving lethal when cultures obtained from these abscesses are injected into other animals. These facts seem to indicate that under certain unknown natural conditions the virus tends to acquire increased potency, whilst in other circumstances its virulence tends to diminish.

This conjecture is countenanced by the results of experiment on animals. It has been shown that by passing the virus by inoculation from one guinea-pig to another the rate of its action becomes accelerated. On the other hand, Yersin remarks that, although it is difficult to start a gelatine-peptone cultivation, nevertheless, when obtained, such a cultivation—at all events certain parts of such a cultivation—will be found to be quite as lethal as virus derived directly from a bubo. He further observed that in such cultures a proportion of the colonies developed more rapidly than others; that if inoculation is made from these more rapidly developed colonies, virulence is found to be diminished; and that if these rapidly growing cultures are frequently repeated, in the long run they cease to be fatal to guinea-pigs, although they may still prove fatal to white mice.

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These and other natural and experimental data indicate a very pronounced tendency to mutability as regards virulence on the part of the plague bacillus: a disposition which, in the future, may very well be turned to important practical account.

Experimental plague.—*Inoculation.*—Intentional and unintentional experiments have proved the inoculability of plague in man. Whyte in 1802 communicated the disease to himself, and died of it. At Cairo, in 1835, two condemned criminals were inoculated from the blood of plague patients; they contracted the disease, but recovered. The value of these experiments, as proving inoculability, is somewhat invalidated by the circumstance that they were made in the presence of an epidemic of the disease. Ordinary methods of infection cannot be said, therefore, to have been absolutely excluded. For the same reason the cases of Aoyama and his assistant, who were believed to have contracted the disease from dissection wounds, cannot be held as proving that plague is inoculable in man. The deplorable accident in a Vienna laboratory, in October, 1898, by which fatal plague of a pneumonic type was acquired, in what way is not exactly known, from manipulations with plague cultures, goes far to complete the little that was wanting in the chain of evidence that this disease is caused by the introduction of the specific bacillus into the human body. The unintentional experiment, in this instance at all events, was not vitiated by having been made in the presence of a plague epidemic.

There is no reason for supposing that man differs in this respect from the lower animals, many of which are exceedingly susceptible to inoculation. Mice, rats, guinea-pigs, and rabbits are invariably killed if successfully inoculated from the buboes* of plague patients. They present on dissection characteristic lesions with numerous bacilli in the

* The pus from a bubo is not always infective. Inoculation made with such may fail. Apparently the bacteria of suppuration may kill out the *Bacillus pestis*.

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lymphatic glands, blood, spleen, and other viscera. Guinea-pigs die in from two to five days after inoculation, mice in from one to three days. Calves and swine are susceptible to inoculation, and so are monkeys and many other animals.

In the case of the guinea-pig, within a few hours of the introduction of the virus a considerable amount of œdema is already apparent around the puncture, and the adjacent gland is perceptibly swollen. At the end of twenty-four hours the animal is very ill; its coat is rough and staring, and it refuses food. Presently it falls on its side and becomes convulsed, one fit following another with increasing frequency as death approaches. If the body is opened immediately after death a rosy-red sanguineous œdema is found at the point of inoculation, with hæmorrhagic inflammatory effusions around the nearest lymphatic gland, which is much swollen and full of bacilli. The intestines are hyperæmic; the adrenals, kidneys, and liver are red and swollen. The much enlarged spleen frequently presents an eruption of small whitish granulations resembling in appearance miliary tubercles. All the organs, and even any serous fluid that may be present in peritoneum or pleura, will be found to contain plague bacilli. In the blood, besides those free in the liquor sanguinis, bacilli are to be found in the mononuclear, though not, it is said, in the polynuclear leucocytes.

Feeding experiments.—Rats or mice fed on cultures of plague bacilli, or on fragments of the liver or spleen of animals dead of plague, acquire the disease, and generally die with the characteristic symptoms and lesions. Similarly, as has been shown recently by Simpson, pigs, calves, sheep, monkeys, hens, pigeons, turkeys, geese, and ducks are affected with plague when fed on plague material. The type of plague induced by feeding is the septicæmic. The disease thus induced is of an acute, or of a chronic nature. When the latter, it may be ill defined and not easily recognised. Thus pigs may show no marked signs of illness until a month after feeding on infective material, and then only a few days or

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hours before death. Susceptibility to plague of the animals of the farmyard, and the chronicity and ill-defined nature of the disease which not unfrequently occurs among these animals, as well as in rats, are likely to be important factors in continuing the disease in those endemic centres where people, cattle, pigs, and poultry, in addition to the ordinary domestic vermin, are housed under the same roof, and even in the same room.

The rat and rat fleas.—Yersin placed in the same cage healthy and plague-inoculated mice. The latter died first; but later the originally healthy uninoculated mice also succumbed; proving that plague is communicable either through the atmosphere, by contact, or by ectozoa.

Fig. 54.—Pulex cheopis.

Yersin's experiment has been successfully repeated again and again, with mice, rats, guinea-pigs, and monkeys, and with many modifications. The result has been indisputable confirmation of Yersin's results, and further proof that plague is not communicable from animal to animal by simple contact or by atmospheric convection, but that it is readily communicated by ectozoa, especially rat fleas—principally *Pulex cheopis*—which act as passive intermediaries and carriers of the bacillus. Zirolia has found that *Bacillus pestis* multiplies in the stomach of the flea, retaining its virulence for seven or eight days and being passed out in the fæces; so that the flea serves not only as a carrier, but also as a multiplier of the germs.

Especially convincing are the experiments of the Indian Plague Commission (*Journal of Hygiene*, Vol. VI., No. 4, April, 1906), which clearly show that if fleas are excluded, healthy rats will not contract the disease even if kept in intimate association with plague-infected rats. Young rats may

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be suckled even by their plague-stricken mothers and remain healthy. But if fleas are introduced, whether naturally or intentionally, into the field of experiment, plague at once begins to spread from rat to rat, and with a rapidity in proportion to the number of fleas present. The commission has shown further that an epizootic of rat plague may start without contact or even proximity of healthy and infected animals. It suffices to transfer fleas from a plague animal on to a healthy animal, or to place the latter in a room in which plague rats had died recently and been subsequently removed. The fleas that had left the body of the dead rats, remaining in the room, convey the germs. The atmosphere of the room is not infective; for if the experimental animal be suspended in an open cage a few feet above the floor, it does not become infected. Nor is the animal infected if placed on the floor, if the precaution be taken to surround the cage with "tangle foot" so as to keep the fleas off. But if it is placed on the unguarded floor, either in its cage or be allowed to run about, or even if it is suspended two inches above the floor—a distance not beyond the saltatory powers of the flea—it will become infected. The commission obtained practically the same results in experiments with guinea-pigs in plague-infected houses. It is therefore no longer open to question that the important—probably the most important—agents in the development and perpetuation of plague epidemics are the rat and the rat flea, *Pulex cheopis*, and other fleas, such as *Pulex canis*, which is known to bite both dog, man, and rat indifferently. This important conclusion is completely supported by the elaborate epidemiological observations of Ashburton Thompson in Sydney, who has shown that the rat-

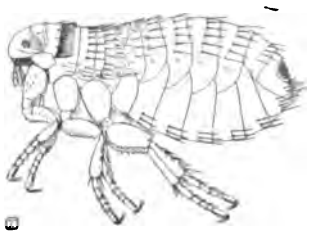

Fig. 55.—Pulex canis (female).

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flea theory best explains the behaviour of epidemic plague—at all events in that city.

Apart from the very serious danger arising from vermin affected with chronic plague, which may hang about a house for a long time, it would appear that the house itself does not retain the infection for any length of time. The Plague Commission has shown that floors of cow-dung if contaminated with *Bacillus pestis* do not remain very infective for more than 48 hours, and that floors of chunam cease to be infective in 24 hours.

The ancients were well aware of the connection between plague and the rat. In the Bible the rat is mentioned in association with the plague which broke out amongst the Philistines after they stole the Ark of the Covenant. The Greeks of Asia Minor worshipped a rat-killing Apollo who was reputed to bring and remove plague epidemics. Sambon describes a coin of Lucius Severus, struck at Pergamum in Asia Minor at the time of a great plague epidemic. On the obverse of the coin is the god of medicine, Æsculapius, having at his feet a dead rat and at his side a naked human figure in an attitude of terror or supplication. Mediæval literature likewise contains abundant proof that the association of rats with plague was well recognised even in the dark ages. Many modern observers also have remarked the great mortality among rats and other animals which generally precedes and accompanies outbreaks of plague in man. Writing about the mortality among rats during the recent Canton epidemic, Rennie remarks that the Chinese regarded this unusual and striking occurrence as a sure indication of an extension of the epidemic. From districts of the city where the plague had been raging for some time the rats entirely disappeared, whilst they kept on dying in other quarters to which the disease afterwards spread. The rats, he says, would come out of their holes, in broad daylight even, and tumble about in a dazed condition and die. In a very short time one Chinese officer alone collected upwards of 22,000 dead rats.

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Rocher states that in Yunnan the mortality among the rats is particularly noticeable. Other animals also die, he says; oxen, sheep, deer, pigs, and dogs are all attacked at times, the dog less severely and less frequently than the others.

Pringle says that in Shurwal, Himalayas, where in 1864 plague was epidemic, the rats quitted the various villages in anticipation of the advent of the disease, and that the people, taught by experience, on seeing this exodus recognised it as a warning.

Clemow has pointed out the connection of Mongolian and Siberian plague epidemics with the occurrence of the disease in a species of marmot, called tarbagan (*Arctomys bobac*), common and much hunted in these regions.

These and many similar facts observed in Bombay, Sydney, Cape Town, and Hong Kong with regard to plague in the lower animals throw important light on one of the ways in which the disease is spread. They, together with the results of the several experiments already alluded to, have to be reckoned with in the future, more than they have been in the past, in devising schemes of quarantine and in attempts at stamping out the disease in already affected localities. The wholesale destruction of domestic vermin should go hand in hand with the isolation of plague-stricken patients.*

Conditions favouring naturally acquired

* It is stated that the handling of a rat newly dead of plague is fraught with danger, whereas a rat that has been dead for some time and is cold and stiff may be touched with impunity; and it is surmised that the fleas of the newly dead rat are still in its fur, and quit it for the body of the manipulator, carrying on their probosces the bacilli of the disease, which they introduce when they proceed to feed on their new host. When a rat has been dead for some time and the body is cold, the fleas have already forsaken it; hence the impunity with which the rat itself may be handled, but the danger of the locality in which it died and where the hungry infected fleas are awaiting an opportunity for a meal. The fact that the glands of the legs are usually the first to become implicated in the majority of cases of plague suggests that the virus is generally introduced through the skin of the feet or legs, which are just those parts most likely to be attacked by a flea picked up in walking across the floor of a room in which plague-stricken rats or other animals have died.

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plague.—The most potent circumstances which predispose to the epidemic outbreak of plague are extreme filth and overcrowding. In such circumstances the virus, once introduced, tends to spread. These conditions, however, are not all-sufficient, for even in the filthiest and most crowded Oriental towns, and without any apparent alteration in the habits or circumstances of the population, the disease, after having become epidemic, dies out spontaneously. It may be difficult to indicate the exact way or ways in which filth and overcrowding operate; but certain it is, as experience has shown, that in sanitary hygienic conditions plague does not spread even if introduced, and that in opposite conditions it may for a time spread like wildfire.

Filth and overcrowding imply close proximity of the sick and the healthy; an atmosphere saturated with the emanations of the sick; a lowered tone of the general health; abundant saturation of soil and surrounding media with animal refuse; abundance of body vermin of all kinds; abundance of other vermin, such as rats and mice, which serve as multipliers of the virus; carelessness about personal cleanliness, about wounds of the hands and feet, about clothing, and about food, dishes, and water. One can understand how in such circumstances the germ has opportunities to multiply and spread.

Except in the case of the relatively rare pneumonic form, plague, though "catching," is not nearly so contagious as are scarlet fever, measles, or small-pox. Medical men, and even nurses, in clean airy hospitals rarely acquire the disease, provided they have no open wounds and do not remain too long in close proximity to their patients. In cities the cleanly districts are generally spared. This was well exemplified in the late epidemics at Canton and Hong Kong where the airy, cleanly European quarters and the relatively clean, well-ventilated boat population were practically exempt, whilst the disease ran riot in the adjoining filthy, overcrowded native houses only a few yards away.

The fact that plague can be communicated to the

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lower animals by feeding them on the tissues of plague patients and on cultures of the specific bacillus, suggests that the disease may be conveyed to man in food or drink. The bacillus is sometimes found in the intestinal contents of patients. It is also to be found in the urine. Water or food contaminated with sewage or fæcal matter may therefore be regarded as a possible medium of infection. Food contaminated by infected rats is likely also to be a source of danger. In the epidemic of 1902, in Hong Kong, plague bacilli were found in the intestinal contents and mucus of the mouth in about one-third of the plague-infected rats examined, and in the urine in about one-fifth of the cases (Simpson).

It would appear that a certain degree of concentration of virus, such as we may assume to exist in direct inoculation into wounds, or a prolonged exposure to concentrated aërially-borne germs, is necessary for successful infection. The bacilli do not, as a rule, penetrate the unbroken epidermis, as proved by the impunity with which *post-mortem* examinations in plague cases have often been made; but it seems not improbable that in a proportion of instances the plague germ is introduced through trifling wounds of the feet. It is conceivable that such germs as may be lying about on the ground, deposited there in the discharges of sick human beings or of plague-stricken animals, or perhaps growing there in natural culture, may be picked up in this way. The frequency with which the primary bubo, as will be pointed out, is located in the deep femoral glands favours this idea. One can understand, too, how lice, fleas, bugs, and perhaps flies might act as carriers of the virus from person to person, inserting it with their bites, or inducing scratching and superficial skin lesions, through which the virus obtains entrance. Yersin found that the flies in his Hong Kong plague laboratory died in great numbers, their bodies being crowded with the specific bacillus; he injected bouillon containing a trituration of one of these flies into a guinea-pig, and the animal presently died with all

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the signs of plague. Sablonowski, who in 1884 in a measure anticipated the discovery of the bacillus by Kitasato and Yersin, remarked that during the Mesopotamian epidemic of that year a certain species of fly appeared and disappeared concurrently with the plague; he considered that this insect was an active agent in spreading the disease.

That the plague bacillus does at times enter the body through the unbroken skin or mucous membrane is made highly probable: (1) by the absence in the great majority of cases of human plague of evidence of an initial skin lesion; (2) by the success of experimental feeding of animals with plague tissues or cultures; (3) by the ease with which infection is conveyed through the air to man and other animals in pneumonic plague; and (4) by the certainty with which rats can be infected by simply smearing a plague culture on the shaven skin.

Age, sex, and occupation have very little influence in plague. The youngest children are susceptible; old age seems to be to a certain extent protective, the disease being rarer after fifty than during adolescence. Women, doubtless on account of their remaining much indoors in the tainted surroundings, are relatively more frequently attacked than men.

Geological constitution of soil appears to have no direct influence on plague.

Atmospheric temperatures if very high or very low seem to have a repressing effect. Thus, as a rule, epidemics in Egypt and Mesopotamia declined during the height of the very hot and dry summer, and in Europe during the extreme cold of winter. On the other hand, plague on more than one occasion has flourished during a Russian winter, and also, as in Hong Kong recently, during the heat of a tropical summer. On the whole, the evidence points to moderate temperatures—50° to 80° F.—combined with a certain degree of dampness as being the principal atmospheric conditions favouring epidemic outbreaks and recurrences. Manifestly any influence temperature may have is only an indirect one.

In large towns, and in some districts, in which

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plague recurs for several years in succession there is a seasonal periodicity (which may not be the same in all places) of maximum and minimum prevalence.

Elevation, as regards sea-level, does not directly affect the general distribution of the disease. Indeed, mountain tribes, probably on account of their poverty and squalor, are peculiarly liable to epidemics. In houses the ground floor is more dangerous than the upper storeys.

The *duration of epidemics of plague* is very variable. In large cities—Bombay, Hong Kong, Canton, for example—when fairly established the disease may not relax its grip for ten or more years. In smaller places it may disappear in a few months.

The *extension of plague epidemics* is peculiar, and in many respects resembles that of cholera. It follows trade routes. Sometimes it spreads rapidly from point to point; more generally it creeps slowly from one village to another, from one street or one house to another. Sometimes it skips a house, a village, or a district, to appear there later. Particular houses, and even particular floors of houses, may be infected, whilst neighbouring ones remain free from the disease.

These and many other facts in the epidemiology of plague are probably to be explained by the connection of the disease with the rat flea. When we have fuller information about the migrations of the rat, the breeding seasons of the rat flea, the influence of food and temperature and other circumstances on these animals, it is reasonable to expect that our knowledge of the principles that underlie the transmission, the spread and decline of plague will be more satisfactory than it is at present.

Symptoms.—*Incubation period.*—Symptoms of plague begin to show themselves after an incubation period of from two to eight days. It is said that in certain very rare instances the incubation period may extend to as much as fifteen days. It is also said that in highly malignant epidemics the disease may declare itself within three or four hours from the time of exposure to infection.

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Prodromal stage.—In a certain but small proportion of cases there is a prodromal stage characterised by physical and mental depression, anorexia, aching of the limbs, feelings of chilliness, giddiness, palpitations, and sometimes dull pains in the groin at the seat of the future bubo.

Stage of invasion.—Usually, the disease sets in somewhat suddenly with fever, extreme lassitude, frontal or, more rarely, occipital headache, aching of the limbs, vertigo, drowsiness or perhaps wakefulness, troubled dreams. Rigor is rarely a marked feature; more often the disease is heralded by feelings of chilliness. The face quickly acquires a peculiar expression, the features being drawn and haggard, the eyes bloodshot, sunken and staring, the pupils probably dilated; sometimes the face wears an expression of fear or horror. The patient, when he can walk, drags himself about in a dreamy sort of way, or he staggers like a drunken man. There may be nausea and vomiting; in some instances there is diarrhœa.

Stage of fever.—The stage of invasion may last for a day or two without a serious rise of temperature occurring. Generally it is of much shorter duration; or it may be altogether wanting, the disease developing abruptly without definite rigor or other warning, the thermometer rising rapidly to 103° or 104°, or even to 107°, with a corresponding acceleration of pulse and respiration. The rise of temperature is more gradual than is usual in malarial fevers. The skin is now dry and burning, the face is bloated, the eyes are still more injected, sunken and fixed, the hearing is dulled. The tongue is swollen and covered with a creamy fur, which rapidly dries and becomes brown or almost black; sordes form on the teeth and about the lips and nostrils. Thirst is intense, prostration extreme, the patient from utter weakness being hardly able to make himself heard. Sometimes the patient becomes delirious; more generally he sinks into a state of typhoid stupor and prostration, perhaps picking the bedclothes or trying to catch imaginary objects. The delirium is some-

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times wildly furious, sometimes fatuous, sometimes of a low muttering type. Coma, convulsions—sometimes of a tetanic character, retention of urine, subsultus tendinum, and other nervous phenomena may occur. Vomiting is in certain cases very frequent; some are constipated, others have diarrhœa. The spleen and liver are usually both enlarged. Urine is scanty, but rarely contains more than a trace of albumin. The pulse, at first full and bounding, in the majority of cases rapidly loses tone, becoming small, frequent, fluttering, dicrotic, intermittent. In the later stages the heart may be dilated, the first sound being feeble or absent. In many cases, as death approaches, there may be some cyanosis.

Stage of adenitis.—In from about two-thirds to nine-tenths of the cases, some time between the first few hours and the fifth day, generally within twenty-four hours, the characteristic bubo or buboes develop. Usually (in 70 per cent.) the bubo forms in the groin, most frequently on the right side, affecting one or more of the femoral glands; less frequently (20 per cent.) it is the axillary glands, and still more rarely (10 per cent.), and most commonly in children, it is the glands at the angle of the lower jaw that are affected. The buboes are usually single; in about one-eighth of the cases, however, they form simultaneously on both sides of the body. Very rarely are buboes formed in the popliteal or in the epitrochlear elbow glands, or in those at the root of the neck. Occasionally buboes occur simultaneously in different parts of the body.

The buboes vary considerably in size. In some instances they are not so large as a walnut; in others they attain the size of a goose's egg. Pain is often very severe; on the other hand, it is sometimes hardly complained of. Besides the enlargement of the gland, there is in most instances distinct infiltration of the surrounding connective tissue.

In a very small proportion of cases what are usually described as carbuncles, but which are in reality small patches of moist gangrenous skin that may gradually involve a large area, develop on

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different parts of the integument. These occur either in the early stage or late in the disease. Sometimes they slough and lead to extensive gangrene.

In favourable cases, sooner or later, after or without the appearance of the bubo, the constitutional symptoms abate with the setting in of a profuse perspiration. The tongue now begins to moisten, the pulse-rate and temperature to fall, and the mild delirium, if it has been present, to abate. The bubo, however, continues to enlarge and to soften. After a few days, if not incised, it bursts and discharges pus and sloughs—sometimes very ill-smelling. In rare instances suppuration is delayed for weeks; whilst in some the bubo subsides after a few weeks, or perhaps months, without having broken down. Convalescence, when it occurs, sets in some time between the sixth and tenth day, although it may be delayed for a fortnight or three weeks. Occasionally a pyæmic condition, with boils, abscesses, cellulitis, parotitis, or secondary adenitis, succeeds the primary fever. The sores left by the buboes and abscesses of plague are extremely indolent, and may take months to heal.

Hæmorrhages of different kinds are not an unusual feature of plague. Ecchymotic effusions of a purplish or dull red tint, and varying in size from a hemp-seed to spots half an inch in diameter, are very often found scattered in greater or less profusion over the skin, especially on exposed parts of the body and at the sites of insect bites or of wounds. Larger patches of cutaneous hæmorrhagic effusion are rare. There may be bleeding from the nose, mouth, lungs, stomach, bowel, or kidneys. Hæmorrhages occur with marked frequency in certain epidemics; they are regarded as evidence of great malignity. Especially malignant are those epidemics in which hæmoptysis, or pneumonia, is a common occurrence.

Abortion almost invariably occurs in pregnant women; the fœtus sometimes shows signs of the disease.

Death may take place at any time in the course of plague. Usually it occurs between the third and fifth day, with symptoms of profound adynamia,

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heart failure, or perhaps from convulsions, from coma, from internal hæmorrhage, or, later, from exhaustion consequent upon prolonged fever or suppuration, or from secondary hæmorrhages.

On the other hand, in a certain proportion of cases convalescence sets in and proceeds more or less rapidly. Generally it is a tedious affair, being prolonged by suppuration, sloughing, and similar complications.

The foregoing description applies more especially to the ordinary *bubonic* (as it is called) type of the disease. Of late, certain forms of plague have received individual recognition in consequence of their extreme virulence and, in the case of one of these forms, of its high degree of communicability. These forms are called respectively *septicæmic* and *pneumonic*.

Septicæmic plague, sometimes called **pestis siderans.**—In this type there is no special enlargement of the lymphatic glands apparent during life, although after death the glands throughout the body are found to be somewhat enlarged and congested. The high degree of virulence and rapid course of the disease depend on the entry of large numbers of the bacilli into the blood, where they can be readily found during life. The patient is prostrated from the outset, he is pale and apathetic; there is no, or very little, febrile reaction (100°). Great weakness, delirium, picking of the bedclothes, stupor, and coma end in death on the first, second, or third day. Frequently in these cases there are hæmorrhages.

Pneumonic plague.—This type of the disease, which was carefully studied by Childe, is especially dangerous as well as deadly: dangerous because of the multitude of bacilli which are scattered about in the patient's expectoration, and because the clinical symptoms are unlike those of typical plague, and are apt to be mistaken for some ordinary form of lung disease. The illness commences with rigor, malaise, intense headache, vomiting, general pains, fever, and intense prostration. Cough and dyspnœa set in, accompanied by a profuse watery blood-tinged

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sputum. The sputum is not viscid and rusty, as in ordinary pneumonia. Moist râles are audible at the bases of the lungs, the breathing becomes hurried, other symptoms rapidly become worse, delirium sets in, and the patient dies on the fourth or fifth day. This is the most fatal, and is said to be the most infectious form of plague.

Abortive or larval plague (pestis minor, pestis ambulans).—Certain epidemics are distinguished by the large proportion of mild cases. In such, buboes form and suppurate or resolve, the associated constitutional symptoms being comparatively mild, or perhaps altogether wanting. In every epidemic there may be cases in which the patient is able to be about, having little if any fever, and apparently being little inconvenienced by the disease. Such cases, however, may collapse suddenly.

The occurrence of epidemics of bubo with little or no constitutional symptoms, which precede and follow true plague, has already been alluded to (p. 270). These cases are of great importance in their bearing on the spread and prevention of the graver disease.

Relapses, though rare, do occur, and are dangerous.

Mortality.—The case mortality varies in different epidemics. It is usually greatest at the beginning and height of the epidemic. Disregarding those mild epidemics just alluded to, the death-rate may be anything from 60 to 95 per cent. of those attacked. Much appears to depend on the social condition of the patient, the attention and nursing available, and on the amount of the initial dose of virus. Thus in a recent Hong Kong epidemic, whilst the mortality among the indifferently fed, overcrowded, unwashed, and almost unnursed Chinese amounted to 93·4 per cent., it was only 77 per cent. among the Indians, 60 per cent. among the Japanese, and 18·2 per cent. among the Europeans, a gradation in general correspondence with the social and hygienic conditions of these different nationalities. In the South American epidemics and in the recent circumscribed

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epidemics in Europe, the mortality was only about one-third of that obtaining in India and China.

Pathological anatomy and pathology.—After death from plague the surface of the body very frequently presents numerous ecchymotic spots or patches. The number and extent of these vary, apparently, in different epidemics. Sometimes—as in the Hong Kong epidemic of 1894 — they are few and trifling, having their origin, as mentioned, principally in insect bites. In other epidemics, according to their historians, the cutaneous hæmorrhages have been both extensive and numerous; hence the name Black Death formerly applied to this disease. The characteristic buboes are generally apparent; occasionally there are also furuncles, pustules, and abscesses. Rigor mortis is usually moderate; sometimes *post-mortem* muscular contractions, like those of cholera, take place. *Post-mortem* rise of temperature is often observed. Decomposition is said to set in early.

The characteristic appearance in a necropsy of plague is that of engorgement and hæmorrhage, nearly every organ of the body participating more or less. There is also parenchymatous degeneration in most of the organs. The brain, spinal cord, and their meninges are markedly congested, and there may be an increase of subarachnoid and ventricular fluid. There are numerous and pronounced puncta cruenta on the brain sections; occasionally there may be considerable extravasations of blood into the substance of the brain (mesocephalon and medulla oblongata).

Ecchymoses are common in all serous surfaces; the contents of the different serous cavities may be sanguineous. Extensive hæmorrhages are occasionally found in the peritoneum, mediastinum, trachea, bowel, pelvis of kidney, ureter, bladder, or in the pleural cavities. The lung frequently shows evidences of bronchitis and hypostatic pneumonia; sometimes hæmorrhagic infarcts and abscesses are found. The right side of the heart and great veins are usually distended with feebly coagulated or fluid blood.

The liver is congested and swollen, and its cells

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are degenerated. The spleen is enlarged to two or three times its normal size. The mucosa of the alimentary canal as a whole is congested, showing here and there punctate ecchymotic effusions and, occasionally, hæmorrhagic erosions, and even—especially about the ileo-cæcal valve—ulcerations.

Similarly the kidneys are congested, and may exhibit ecchymoses, both on the surface and in the pelvis. The perirenal connective tissue also may be congested and infiltrated. The ureters and the mucous surface of the bladder are often found to be sprinkled with ecchymoses, in which cases the contained urine is generally bloody.

Evidence is invariably discoverable of serious implication of the lymphatic system. One, two, or many of the lymphatic glands are inflamed and swollen. Both in and around the glands there is much exudation with hæmorrhagic effusion, hyperplasia of the gland cells, and an enormous multiplication of bacteria. The glands of the groin, of the armpit, and of the neck are particularly affected. On dissection, the superficial buboes are very often found to be connected with extensive, deep-seated adenitis extending either through the crural ring or down the neck, and involving the pelvic, the abdominal, or the mediastinal glands as the case may be. Section of the affected glands will reveal any stage of inflammation from cellular hyperplasia to suppurative softening, according to the period of the disease at which death has occurred. In whatever stage death has taken place, there is always evidence of intense hyperæmia in, as well as around, these glands—a hyperæmia which is specially characterised by a marked tendency to hæmorrhagic effusion. In the earlier stages of the adenitis the specific bacillus is found in the lymph spaces around the follicles; later, it is found in the follicles themselves, in the lymph spaces, and in the medullary cords (Aoyama).

If death has taken place at a very early stage of the disease, the swelling of the lymphatic glands may not be so evident; but it is rare not to find some gland or glands characteristically affected. In those

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septicæmic and pneumonic cases in which the bubo is absent, nearly all the lymphatic glands of the body are slightly enlarged, pink or dark red in colour. Instead of intense and localised adenitis, a milder but more general enlargement of the lymphatic glands of the entire body is discovered. Sometimes the lymphatic trunks are also markedly implicated.

Diagnosis.—The occurrence of fever and adenitis during a plague epidemic must always be viewed with suspicion, particularly if the fever rapidly assumes an adynamic character. In the early stages diagnosis may be very doubtful, especially in pneumonic plague. The discovery of the bacillus in the glands, blood, sputum, or discharges is the only thoroughly reliable test. A small quantity of the suspected material should be spread on a slide, dried, fixed, and stained with an aniline dye. Should a cocco-bacillus be found with the characteristic bi-polar staining, it should be cultivated by Haffkine's method in broth on which clarified butter (ghee) or cocoanut-oil is floated. From the under surface of the oil, if the bacillus be that of plague, stalactite-like growths of bacilli will form. When disturbed, the stalactite growths break off and fall in snow-like flakes to the bottom of the vessel. No other known bacillus behaves in this way.

General prophylaxis.—The prophylaxis of plague, as of other infectious diseases, has to be considered from the standpoint of the community and also from that of the individual. As regards the former, it includes measures for preventing the introduction of the virus, for staying its spread if introduced, and for securing its destruction.

Quarantine.—Modern systems of land or sea quarantine directed against plague take cognisance of the facts that the incubation period of the disease may extend to ten days, and that plague affects certain of the lower animals as well as man. Ten days is the minimum period that should elapse between the time of departure from an infected place, between the date of the last death, or between the arrival of a ship or batch of travellers with cases

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of plague in progress among them, and free pratique. Moreover, as Kitasato has shown that the specific bacillus persists in the bodies of those who have recovered from plague for at least three weeks from the cessation of the active disease, convalescents should be isolated for a month before they are allowed to mingle with an uninfected community.

Although Kitasato has stated that the plague bacillus perishes in four days when dried on cover-glasses and protected from sunlight, and in from three to four hours when exposed to sunlight, experience has shown that under certain conditions, as yet unknown, it will survive outside the body for a very much longer period. There is a considerable mass of evidence tending to show that clothes, skins, textile fabrics, and other similar materials may preserve the virus in an active state for several months. Such articles, therefore, coming from an infected district, more especially if there is any suspicion that they have been soiled by, or have been in proximity to, plague patients, should be destroyed or thoroughly disinfected.

In ships coming from an infected port the rats, mice, and such-like vermin should be destroyed, thrown overboard, and sunk before harbour is entered. The generation of sulphurous acid gas under pressure, especially the Clayton system, has been found useful for this purpose.

Kitasato found that bouillon cultures of the bacillus were killed in half an hour by a temperature of 80° Cent., and in a few minutes by steam at 100° Cent. Growth of the bacillus did not occur in cultures after exposure for one hour to a 1 per cent. solution of carbolic acid. The bacilli are also killed by a three hours' exposure to milk of lime. These facts serve as a guide to suitable disinfectants, of which the best and most practicable are steam, 1 in 1,000 corrosive sublimate in carbol-sulphuric acid; lysol, chloride of lime in 1 per cent. solution, carbolic acid in 5 per cent., formalin 2 per cent.

On plague breaking out in a small village community, so soon as the disease is recognised measures

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should be taken to prevent the inhabitants leaving the locality, and thus spreading the disease. There is little danger of this until the inhabitants become alarmed by a rapid extension of the disease. If possible, after the patient has been isolated in a special hospital, the village should be evacuated for a month, the inhabitants being accommodated in temporary huts close by, while the houses which the patients have occupied and those in their neighbourhood should be disinfected. The safest and most thorough form of disinfection is by fire, and in the case of an isolated village prompt destruction of the infected houses by fire is the surest method of stamping out the infection. The clothes and bedding of all patients should be burned. The dead, with as little delay as possible, should be buried in deep graves or cremated. Isolated observation camps should be organised, in which "suspects" and "contacts" may be segregated for a time equal at least to the incubation period of the disease. Rats and mice should be poisoned or otherwise destroyed, and their bodies burned. Besides such special measures, general sanitation should be scrupulously carried out. The diffusion of plague by railways must be carefully guarded against.

In the event of an outbreak in a town, it must be borne in mind—first, that there is an intimate connection between rat plague and human plague; second, that rat plague is conveyed to human beings, and, once established in human beings, is communicable to others and to rats by means of the expectoration, by the discharges from the bowels and by the urine, and by discharges from the buboes or glandular swellings; and third, that a plague in rats usually precedes plague in human beings. It is as important to know in what houses, areas, and quarters of the town the rats are infected as it is to know in which of these there are plague patients. In addition, therefore, to prompt notification of plague patients, a system is required to obtain information as to plague rats. It is not sufficient to carry on a general campaign against rats, and to

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burn all rats which have been poisoned or caught in traps, but it is necessary to examine daily bacteriologically every rat so destroyed, in order to determine whether it is healthy or infected, and so to differentiate the healthy parts of the town from the infected. A ticket on the rat, giving the address from which it was brought, locates the street and house, and permits of action being taken at once. A house in which a plague rat is found is a plague-infected house, and if plague among the inmates is to be prevented, the necessary preventive measures should be taken at once. These measures consist in the evacuation of the house until it has been disinfected and rendered rat-proof, and the disinfection of the clothes and belongings of the inmates.

In India the compulsory inspection of all dead bodies prior to burial has been found a valuable measure for discovering infected houses and localities.

In all efforts to control the introduction and spread of plague, cases of *pestis ambulans* must be sought out and treated with as much respect as the more virulent forms of the disease.

It is very questionable if in practice any system of rigid quarantine, no matter how carefully devised and theoretically perfect, is ever absolutely protective. Its working is necessarily at the mercy of a large number of individuals, any one of whom, either from incompetence or from dishonesty, may permit its regulations to be broken through. Even if the introduction of plague by man could be prevented in this way, it is difficult to see how its introduction by rats or mice could be effectually guarded against. Quarantine may, and doubtless does, keep out a proportion of the infected, and to this extent it does some good; but it must be combined with careful general sanitation, with thorough disinfection, with the destruction of all discharges and fomites, with the speedy discovery and isolation of the sick, with the evacuation of infected houses and even of neighbourhoods, and with the wholesale destruction of vermin. These latter things English experience has shown to be far more effective than any system of

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quarantine; it was only in deference to Continental views that quarantine, in the ancient sense of the word, was practised in Great Britain against plague and yellow fever. A rational quarantine plus rational sanitary measures is what is wanted.

Destruction of vermin and other measures in anticipation of the introduction of plague virus.—Considering the well-established facts that rats are specially susceptible to plague, that in many epidemics they have been attacked weeks before the disease has shown itself in man, that their habits bring them into intimate association with man, there can be no doubt that these rodents play a very important part in the diffusion of the introduced virus. This being the case, it is reasonable to believe that if the rats were destroyed the risk from the introduction of a case of plague, whether by man, rat, or fomites, would be very much reduced in any community in which this measure had been carried out. The responsible authorities of all towns and villages in active communication with plague centres should, *in anticipation* of the possible advent of the infection, see to the destruction of all rats in their districts, and this in addition to instituting the ordinary measures for dealing with overcrowding, food and water supply, domestic and municipal cleanliness. The destruction of rats is a cheap measure in comparison with those adopted in India and elsewhere, which have so signally failed to arrest epidemic plague. The campaign against rats is usually carried on by the employment of rat-traps and rat-catchers, and the laying down, under precautionary conditions, of poisons such as arsenic and phosphorus. As no one method is satisfactory, it is usual to employ several at the same time. The pumping of SO_2 gas under pressure is useful for ships full of cargo and for warehouses with goods in them. So long as the sulphurous acid gas is dry, and is not used on damp articles, no damage is done to merchandise. Care has, however, to be taken with damp things, as they may get slightly discoloured.

Attempts have been made to set up an epidemic

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among the rats which should not be communicable to man. For this purpose the bacillus discovered by Danysz was recommended by him. But the method employed of inoculating a few rats with the bacillus and then allowing them to escape, with the hope that when they sickened they would be eaten by other rats, which would in their turn be taken ill, and an epidemic be thus set up, has not been successful. Experiments on these lines have failed. The Danysz bacillus was, however, found to be useful in Cape Town and elsewhere for the destruction of rats when a system introduced by Professor Simpson was adopted, and bread soaked in the cultures was distributed and laid down in the same way as is usually done with biscuits on which rat poison is spread. By distributing thousands of doses an excellent result was obtained, and rats which were examined in the localities where the Danysz bacillus had been used in this way were found to have died from the disease induced by this organism. Rats which had migrated were also found to have died of the same cause in localities other than those in which the cultures were placed. An important point in the success attending these operations was found by Dr. R. W. Dodgson to be the raising and maintenance of the virulence of the cultures. Those sent out from Pasteur's laboratory after a fortnight's voyage were found to be useless, and consequently required to be exalted in virulence by a series of passages through healthy rats.

Personal prophylaxis.—As regards the individual, all unnecessary visits either to plague patients or to plague neighbourhoods should be avoided and, if possible, prevented. The attendants on the sick ought especially to take care that the ventilation of the sick-room is thorough, that cubic space is abundant, and that the utmost cleanliness is practised. Nurses must not hang over patients unnecessarily; they must also be careful to seal up and cover any wounds, no matter how trifling, they may have on their hands; they must go into the open air frequently, and not remain in the wards too many hours at a

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stretch; they must employ disinfectants freely on themselves and on the excreta of their patients, and use a disinfectant mouth-wash from time to time; they must be careful to wash hands and face before eating, and they must never partake of food or drink in the ward or sick-room. By carefully observing these common-sense precautions, the risk in nursing plague patients is very much reduced, and is certainly very much less than that attending the nursing of cases of typhus exanthematicus. To obviate risk from wounds and to prevent the access of fleas and similar suctorial insects, those engaged on plague duties should wear boots and have the legs protected by trousers tied tightly round the ankles or, better, by putties. Leather gloves are advisable if there is much handling of furniture or of anything likely to abrade the skin. Hospital work is only dangerous when patients are allowed to lie in their dirty flea, louse, or bug infested clothing, when disinfectants are not properly used, and when attendants are careless, stupid, or rash, or where the wards, in the matter of light and ventilation, are by their construction ill adapted for plague cases, and where a number of pneumonic cases are crowded into a single apartment. Cats or dogs should not be allowed near plague patients.

Haffkine's inoculations.—Early in the Bombay epidemic Haffkine introduced a system of prophylactic inoculation which is of proved value, both in reducing the number attacked with plague to the extent of from 77 to 85 per cent. and, also, in diminishing the mortality in those attacked by 80 per cent. A description of Haffkine's methods will be found in the *British Medical Journal* of June 12th, 1897. It consists essentially in the subcutaneous injection of cultures of plague bacilli killed by heat. The reaction is at times severe, but until quite recently no grave accident had occurred. The figures are not so favourable for Mauritius, where inoculations reduced the plague incidence to the extent of 45 per cent. only, and the mortality in those inoculated to 32·9 per cent. The first Indian Plague Com-

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mission reports in favour of these inoculations, but remarks that the vaccine requires more accurate standardising and more accurate dosage to secure the best results. The prophylactic needs great care in its preparation. Its storage in hermetically sealed bottles should be insisted upon, and every bottle ought to be tested before use.

Lustig's injections.—Lustig and Galeotti have introduced a method of preventive inoculation which apparently obviates many of the drawbacks of Haffkine's. They dissolve agar-agar plate cultures of *Bacillus pestis* in 1 per cent. solution of caustic potash, precipitate the nucleo-proteids so dissolved by weak acetic or hydrochloric acid, collect the precipitate, wash and dry it *in vacuo*. This substance, apparently, can be kept for an indefinite time. The dose for a man is about 3 mgrs. Before injecting it subcutaneously, it is dissolved in a convenient quantity of 0·5 per cent. solution of carbonate of soda. Its injection is followed by marked local and general reaction, and in the case of the lower animals by at least temporary immunity from plague. Favourable results have been obtained in man.

Klein has recently advocated a prophylactic prepared by drying plague spleens at 47° C. over sulphuric acid. Ten to 15 mgrs. of this protects rats against virulent plague injections.

Treatment.—Hitherto the treatment of plague has been mainly symptomatic. In attempting to relieve symptoms the asthenic tendencies of the disease must ever be borne in mind, and depressant remedies of all kinds carefully avoided.

During the earlier stages, when headache and perhaps high fever are urgent, much relief may be obtained from ice-bags to the head and neck. If it be deemed advisable to attempt to lower the temperature, sponging of the body every hour with warm water is a much safer measure than the employment of such antipyretics as antipyrin and similar drugs. Vomiting, according to Lowson, is usually relieved by a full dose of calomel followed by a saline. If this does not succeed, or if diarrhœa be present, he recom-

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mends ice pills and an effervescing mixture containing morphia and hydrocyanic acid. Sinapisms to the epigastrium are also useful. Later, when the pulse begins to fail, the same authority recommends strychnia, with or without carbonate of ammonia, in preference to digitalis or strophanthus. Strychnia, he says, should be used as a routine treatment, and commenced early in the disease. In collapse, stimulants of various kinds, including strong ammonia to the nostrils and ether hypodermically, are indicated; they sometimes succeed in resuscitating a sinking patient. Given with judgment, Lowson found that morphia was by far the best hypnotic. At the commencement one-eighth to half a grain hypodermically relieves suffering and procures sleep; later, one-eighth of a grain suffices. Hyoscine (one two-hundredth to one seventy-fifth grain) or chloral (twenty grains) and bromide of potassium (thirty grains) are of service for the same purpose. Diarrhœa, if urgent, is best treated by intestinal antiseptics, as salol in 10-grain doses every four hours. The buboes in the early stage may be treated with applications of glycerine and belladonna. Should they become red and inflamed they must be poulticed and, on softening occurring, incised and dressed with iodoform. Indolent bubonic swellings should be treated with iodine liniment. Feeding and stimulation are to be conducted on ordinary principles.

Serumtherapy.—Yersin, Calmette, and Borrel have shown that intravenous, intraperitoneal, and subcutaneous injections of gelatine cultures of plague bacillus mixed with a little bouillon and heated for one hour to 58° C., if employed in doses just short of producing a fatal issue, and repeated three or four times at intervals of fifteen days, render rabbits immune to the plague bacillus. The heating kills the bacillus but does not destroy its toxins, which at first give rise to a very smart but, with each repetition of the injection, diminishing reaction. They further found that the serum of an immunised animal, if injected into an unprotected rabbit, exercised both an immunising and a therapeutic influence. An unpro-

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tected rabbit was inoculated with a virulent culture of the bacillus, and twelve hours afterwards with the serum. The progress of the disease, which would otherwise have certainly proved fatal, was at once arrested, and the animal recovered. They then immunised a horse by intravenous injections of living virulent cultures. After several injections made at intervals (the second after twenty days), they found that reaction, from being intense, became shorter and less pronounced, and that the serum of the animal was now both preventive and curative of inoculated plague in rabbits, guinea-pigs, and mice.

Accounts had led us to infer that the value of this discovery was practically established for man. Of twenty-six cases of plague in China treated with Yersin's antipest serum, twenty-four are reported to have recovered. Further experience in India, Hong Kong, and elsewhere has not confirmed these brilliant results, the serum treatment of plague both by Yersin's and a number of other sera having so far proved a complete failure.

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CHAPTER XIX

MALTA OR MEDITERRANEAN FEVER

(*Febris undulans*, Hughes)

Definition.—Malta fever—a disease of low mortality, indefinite duration, and irregular course—is the result of infection by a specific germ, the *Micrococcus melitensis*. In its more typical form it is made up of a series of febrile attacks, each individual attack, after lasting one or more weeks, gradually subsiding into a period of absolute or relative apyrexia, also of uncertain duration. Common and characteristic complications are rheumatic-like affection of joints, profuse diaphoresis, anæmia, liability to orchitis and neuralgia.

Geographical distribution.—Malta or Mediterranean fever is somewhat unfortunately named, for we now believe that the disease so designated is not, as was formerly supposed, confined to Malta, or to the Mediterranean even. It is very common there, particularly in Malta and the eastern and southern littoral of the Mediterranean; but recent investigations show that it occurs in the Red Sea littoral, India, China, South Africa, Somaliland, the West Indies, the Brazils, the United States, and even in England. I have seen two cases which originated in England; they gave the serum reaction. It is highly probable, therefore, that the same, or a similar, fever occurs in many other parts of the world, having been confounded hitherto with malarial fever or with typhoid. This conviction is based rather on clinical than on laboratory observation. Experience has taught me to place little reliance on the serum reaction test as ordinarily applied. Although with fresh blood and reliable cultures the reaction may be trustworthy, with stale blood and questionable cultures this test is most untrustworthy. Time after time, in

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London, I have got contradictory laboratory reports on blood from the same patients, presumed to have Malta fever. If the cultures in the London laboratories be so manifestly unreliable, it is probable that many of those in use in India and America are equally so, and that inferences as regards the geographical distribution of this disease, founded on the behaviour of these cultures with blood serum, are most untrustworthy.

As it is extremely prevalent at times in the Mediterranean fleet and in the garrisons of Gibraltar and Malta, this disease is specially interesting to naval and military surgeons. Although only occasionally proving fatal, it is a fruitful source of inefficiency and invaliding.

Until recently it appeared to be on the increase in its old haunts, and to be becoming common in places where it was formerly rare—Port Said and Egypt, for example.

The following figures, supplied by Bassett-Smith, show its importance to our Naval and Military Services in the Mediterranean:—

INCIDENCE OF MALTA FEVER.

	Army.			Navy.		
	Strength.	Cases.	Deaths.	Strength.	Cases.	Deaths.	Total days' sickness.
1900	9,203	171	10	14,250	356	6	22,998
1901	9,384	288	10	14,070	286	3	16,987
1902	10,889	198	10	18,470	436	3	27,432
1903	10,608	507	11	18,410	400	6	30,541
1904	10,615	429	15	19,590	430	9	28,458

History.—Formerly Malta fever was confounded with typhoid and malaria. The labours of clinical observers from Marston (1861) to Maclean (1885), and more especially the bacteriological researches of Bruce (1887), Hughes, Gipps, Wright, Semple, and Bassett-Smith have established it as a special disease. Quite recently an important advance of great practical value has been made by a Royal Society Commission, which has shown that the germ of Malta fever infests several of the lower animals, especially goats, in whose milk and urine it is excreted.

Ætiology.—Bruce, in 1887, demonstrated the

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presence in the spleen in Malta fever of a special bacterium—the *Micrococcus melitensis*, and by a series of experiments proved that it was the cause of the disease. Unfortunately the bacterium occurs only sparsely in the general circulation (unless in the earlier stages, when the temperature is high), and therefore the discovery is of little direct use in diagnosis; but pathologically it is of great importance, as it enables us to say positively that this so-called Malta fever is a distinct disease, altogether different from either typhoid or malaria. The organism is present in abundance in the spleen pulp, and also in the lymphatic glands, in which it persists longer than elsewhere, and from both of which it can be separated by cultivation. Bruce found it in the spleen in ten fatal cases. His results have been confirmed by Hughes, Gipps, Wright, Durham, Bassett-Smith, and others. Injections of pure cultures give rise to a similar disease in monkeys and other animals, from whose blood the micrococcus can be recovered, cultivated afresh, and, on injection into other animals, will again give rise to the disease. In five recorded instances inoculation, intentional and accidental, of cultures of the micrococcus into man has been followed by the characteristic symptoms of Malta fever after an incubation period of from five to fifteen days.

The *Micrococcus melitensis* measures ·33 micro-millimetre in diameter. It occurs generally singly, often in pairs, sometimes in fours, but never, unless in culture, in longer chains. According to Gordon it possesses one to four flagella. It is readily stained by a watery solution of gentian violet, and is best cultivated in a $1\frac{1}{2}$ per cent. very feebly alkaline peptonised agar beef jelly; in this medium, soon after inoculation, it appears as minute, clear, pearly specks. After thirty-six hours the cultures become a transparent amber; later they are opaque. No liquefaction occurs.

At one time believed to be a delicate organism, recent investigations have shown that the micrococcus can live for a long time in water, in dust, or

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on the clothes of patients, and that it is not killed by cold or desiccation. Moreover, it is now known that it is excreted in the urine, and that it occurs in great abundance in the milk and urine of apparently healthy goats (50 per cent.) and cows, and in the urine of apparently healthy men. It is also found in dogs (9 per cent.), sheep, and horses. These facts account in part for the great frequency and dissemination of the disease in such insanitary places as Malta, to which place they specially refer.

Influence of age and residence.—The most susceptible age as regards Malta fever is between the sixth and the thirtieth year. Length of residence does not influence susceptibility. The natives suffer as well as visitors.

Influence of season.—In Malta and other places where the disease is endemic this fever occasionally assumes an epidemic character. The period of its greatest prevalence in Malta is the season of lowest rainfall, embracing June, July, August, and September; differing in this respect from typhoid, which, in that island, is more prevalent during the succeeding months. It is not confined absolutely to the summer months; cases occur all the year round.

Local causes.—The disease tends to occur in particular towns or villages, in particular houses, barracks, hospitals and rooms, and in particular ships, manifestly originating in limited foci of infection. The weight of evidence was regarded by some as pointing to its diffusion by air currents, and not by food or water. There is no absolute certainty on these points. Evidence is rapidly accumulating to show that milk is the most important medium.

Formerly it was supposed that Malta fever was linked to the immediate seashore, and that the sewage-laden, tideless condition of the harbour at Valetta was somehow responsible for its prevalence there. Lately, Zammit has shown distinctly that the disease occurs all over the island, and in some instances is more prevalent in certain inland and relatively sanitary villages than in more insanitary towns and villages on the coast. Certain ships are

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notoriously foci of the disease, and, I believe, can carry the infection. Some time ago I saw a medical man suffering from a chronic fever whose blood, in expert hands, gave the Malta fever reaction, and who, if he had Malta fever, certainly got it from a ship which had recently been to the Mediterranean. He himself had never been in that part of the world, and had not been out of England for a year.

Influence of social conditions.—All classes are liable to this disease; the officer and his family as well as the soldier in barracks or the sailor on shipboard.

Mode of infection. — Although the possibility must not be ignored, Malta fever is not generally transmitted directly from one person to another; that is to say, is not usually directly communicable from the sick to the healthy. The germ is readily conveyed by inoculation; the prick of a contaminated needle will suffice. Zammit and others seek to incriminate the mosquito as an inoculator, and point in support of their contention to the special prevalence of the disease in the mosquito season, to the facts that in 896 mosquitoes examined bacteriologically it was found in 4, and that the disease has twice been conveyed to monkeys by infected insects.

A very striking circumstance is that in some hospitals the nurses and attendants in the fever wards are ten times more liable to contract the disease than people not so employed.

Possibly the infection is blown about by winds as dust, and being inhaled, or falling into the conjunctival sac, or on a wound or sore, obtains an entrance. Bearing in mind the presence of the germ in the excreta of man and animals, the dusty character of the soil of Malta, the extremely minute dose of a culture required for a successful inoculation, in any or all of these ways infection seems possible. I have seen a case, originating in England, in which a father was apparently infected by placing in his mouth the clinical thermometer used by his son recently invalided from Malta on account of the disease.

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It has been suggested that the infection may be conveyed in milk, in other food, or in water. Water as a usual medium may be dismissed, but there is strong evidence, as I have said, against milk, although apparently, judging from naval and military opinion, it is not the only medium. There are facts that point very distinctly to goats' milk as the most important medium of infection. In 10 per cent. of the milk of Maltese goats the micrococcus is present. Monkeys are easily infected by feeding them on such milk. Immediately on the goats' milk supply to the naval and military hospitals in Malta being stopped the cases of locally acquired Malta fever practically ceased. Formerly this fever was very common in Gibraltar. The milk supply of the garrison at that time was largely from goats imported from Malta. Gradually these goats have died out or been got rid of, and no more Maltese goats have been imported. Concurrently with this there has been a marked and proportional reduction of Malta fever cases in the garrison. In 1905 the s.s. *Joshua Nicholson* shipped 65 goats in Malta. An epidemic of Malta fever broke out on board, nearly all those who drank the milk of the goats being attacked.

Immunity.—Bruce holds that one attack confers immunity from subsequent attacks; other authorities believe that one attack, so far from conferring immunity, actually predisposes to subsequent attacks. The latter is Bassett-Smith's opinion, based on the fact that he finds the bactericidal power of the serum and the phagocytic energy of the leucocytes lowered during, and for some considerable time after, an attack of the disease.

Incubation period.—The period of incubation in the naturally acquired disease is difficult to fix. Cases have occurred as early as six days after arrival in Malta; on the other hand, the disease has shown itself as late as fourteen and seventeen days after the subject of it has quitted Malta. Some have held that it may remain latent for months.

Symptoms.—Malta fever begins generally with lassitude and malaise, such as we associate with the

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incubation of many specific fevers, particularly typhoid. There is headache, boneache, anorexia, and so forth. At first the patient may go about his work as usual. Gradually the daily task becomes increasingly irksome, and he takes to bed. Headache may now become intense, and, in addition, the patient will suffer from thirst and constipation. At the commencement the symptoms, with the exception that there is very rarely diarrhœa, resemble those of typhoid. There are no rose spots, however, then or at any subsequent period. There is evidence in the coated tongue, the congested pharynx, the anorexia, and the epigastric tenderness, of gastric catarrh; and the occasional cough and harsh, unsatisfactory breathing at the bases of the lungs indicate some degree of bronchitis or of pulmonary congestion. There may also be delirium at night. The fever is usually of a remittent type, the thermometer rising towards evening and falling during the night, the patient becoming bathed in a profuse perspiration towards morning. The spleen and the liver, but especially the former, are somewhat enlarged and, perhaps, tender. Lumbar pain may be urgent.

After a week or two of this type of fever, specially distinguished by pains and perspirations, the tongue begins to clean, and the appetite to revive; but, notwithstanding these signs of amendment, the patient still remains listless and liable to headache and constipation. He continues feverish and at times perspires profusely. Gradually, however, although the patient is anæmic and weak, subjective symptoms become less urgent; he sleeps well now, he has no delirium at night, and he can take his food, and this although the body temperature may still range slightly above the normal. Then once more, and perhaps over and over again, fever with all the former symptoms gradually returns; and now, if it has not declared itself before, the peculiar fleeting rheumatic-like affection of the joints so characteristic of the disease shows itself in a large proportion of cases. One day a knee is hot, swollen, and tender; next

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day this joint may be well, but another joint is affected; and so this metastatic, rheumatic-like condition may go on until nearly all the joints of the body have been involved one after the other. The patient may suffer also from neuralgia in different nerves—intercostal, sciatic, and so on. Orchitis is an occasional complication. In some cases these complications are severe and characteristic; in others they may be mild, or absent altogether. In this respect the same infinite variety exists as in other specific fevers.

Perhaps the most characteristic feature of Malta fever is the peculiar behaviour of the temperature. In a mild case there may be a gradual ladder-like rise through a week or ten days to 103° or 104°, and then, through another week or so, a gradual ladder-like fall to normal, the fever, which is of a continued or slightly remitting type, leaving for good without complication of any sort in about three weeks. Such mild cases are the exception. Usually, after a few days of apyrexia, absolute or relative, the fever wakes up again and runs a similar course, the relapse being in its turn followed by an interval of apyrexia, which is again followed by another relapse; and so on during several months. This is the "undulant" type from which Hughes derived the name he suggested for the disease—*febris undulans*.

In another class of case a continued fever persists for one, two, or more months, with or without the usual rheumatic, sudoral, and other concomitants—the "continued" type of Hughes.

Generally remittent or nearly continued in type, in a proportion of instances the fever exhibits distinct daily intermissions, the swinging temperature chart suggesting some septic invasion or a malarial fever. But there is no local evidence of suppuration to be found; neither, if we examine the blood, is the malaria parasite to be discovered; nor is the quotidian rise of temperature accompanied by any ague-like rigor, or at most only by a feeling of chilliness; nor is the disease amenable in any way to quinine. This is the "intermittent" type of

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Hughes. In other instances these types may be variously blended.

In some patients, not months merely, but years, may elapse before they are finally rid of the tendency to febrile attacks and characteristic pains and aches. According to Bassett-Smith, the average duration of the disease is four months. Many of our sailors and soldiers are permanently invalided from the services on account of prolonged or recurring types of Malta fever.

Sequelæ and mortality.—As a rule, by far the most serious consequences of Malta fever are the debility it entails, the emaciation, the profound anæmia, the rheumatic-like pains, the neuralgiæ, and such sequelæ as abscess, orchitis, mastitis, parotitis, boils, etc. There is little risk to life; the mortality does not exceed 2·5 to 3 per cent.

When death occurs it is usually from suddenly developed hyperpyrexia; occasionally it is brought about by exhaustion, by hæmorrhages and purpuric conditions, or by some pulmonary complication such as pneumonia. In a few instances the fever is of a fulminating type, rapidly ending in death from hyperpyrexia. Hughes, in his elaborate monograph, designates such cases "malignant."

Pathological anatomy and pathology.—This disease has almost no pathological anatomy. The spleen is the only viscus of which it can be said that it is distinctly diseased. In Malta fever this organ is enlarged (average 17 ounces), soft, and diffluent; on microscopical examination the lymphoid cells are found to be increased in number. There may be some congestion and even ulceration of the intestinal mucosa, but this is not an essential feature.

Diagnosis.—The diagnosis of Malta fever from typhoid is an important practical matter. It is exceedingly difficult in the early stages. Principal reliance has to be placed on the presence or absence of rose spots, of diarrhœa, of joint complications, of sweats, the locality where and the season in which the disease was contracted, and, if available, the agglutination and precipitation tests.

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Wright has shown that, both as regards sedimentation and agglutination, the germ of Malta fever reacts to the serum test in the same way as, and even more markedly than, *Bacillus typhosus*. A weaker dilution (never less than 1 in 30 or 50) than in typhoid must be used. Dead cultures give the reaction, and can be conveniently kept in stock for diagnostic purposes. These observations have been abundantly confirmed. The agglutination reaction appears early in Malta fever as compared with typhoid, being available for diagnostic purposes by the end of the first week of the fever. It persists long after convalescence, often for years.

After the fever has gone on for several weeks diagnosis is, of course, easier; in the early stages, on clinical grounds alone, and apart from the agglutination test, it may be almost impossible. It may be that it is only on the *post-mortem* table that we have the relative assurance, from the absence of ulceration in the ileum, that we have had to deal with a case of Malta fever. Cultures from spleen pulp, with subsequent inoculation into animals, should give reliable evidence if the results are positive. Tuberculosis, abscess, empyema, malaria, relapsing fever, and all causes of continued high temperature of a septic type have to be carefully excluded in attempting a diagnosis. The possibility of the concurrence of another infection, typhoid for example, must not be overlooked.

Prognosis.—In the present state of our knowledge it is impossible to say how long any given case of this disease may last, what the risk to life may be, or what complications may be encountered. Birt and Lamb, from a series of valuable observations, conclude that important deductions may be derived from the behaviour of the agglutinating substances present in the blood. Their conclusions are, briefly, as follow: (1) Prognosis is unfavourable if the agglutinating reaction is persistently low. (2) Also if the agglutinating reaction rapidly fall from a high figure to almost zero. (3) A persistently high and rising agglutinating reaction sustained into

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convalescence is favourable. (4) A long illness may be anticipated if the agglutination figure, at first high, decreases considerably. These conclusions are borne out by Bassett-Smith's recent very careful work.

Treatment.—Malta and those Mediterranean ports in which this fever is endemic should be avoided by pleasure- and health-seekers during the summer. Those who are obliged to live there all the year round would do well, at this season, to leave the towns and reside in places of healthy repute in the country. As a matter of precaution, in the endemic area the drinking water, food, and drains ought at all seasons to receive special attention. All milk should be avoided, or sterilised by boiling. Food dishes should be washed with boiled water. Every care should be taken to avoid insect bites and other skin lesions. Laboratory workers must be careful in handling cultures of the micrococcus; the accidental introduction of the micrococcus into the conjunctival sac has sufficed to cause the disease.

When the diagnosis is sure, it is well to give a purge—none better than calomel and jalap—and to instruct the attendants to keep the patient's temperature systematically below 103° by cold sponging with vinegar and water or, if necessary, by cold bath or ice variously applied. In view of the prolonged nature of the fever, this measure is one of importance; at the same time, such treatment need not be applied too energetically, or so as to depress; a fall of 2° or 3° is all that is desirable.

Quinine and, on account of the joint affection, the salicylates are very generally prescribed. Both are useless, if not injurious. Phenacetin and similar antipyretics are also often given to bring down temperature; but the wisdom of employing depressing drugs in so chronic and asthenic a disease as Malta fever is, to say the least, questionable. Any threat of hyperpyrexia is best met as directed, namely, by early employment of sponging, the wet pack, or, if necessary, by the cold bath. Sleeplessness may demand hypnotics; headache, if severe, moderate doses of phenacetin; inflamed joints or testes, the

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usual local applications; constipation, enemata or aperients. In fact, the treatment of Malta fever resolves itself into a treatment of symptoms.

The therapeutic employment of *vaccines* of dead *M. melitensis*, prepared and administered according to Wright's methods, have been favourably reported on by Reid. In Bassett-Smith's hands the results have not been so favourable. After a prolonged and very careful trial, the latter concludes that if used during the acute phases of the fever, so far from doing good, they act detrimentally; but that in chronic cases, with slight relapses and low temperatures, by stimulating slightly the machinery of resistance they are of real value, and it is to this type of case that he now restricts their use.

The *diet* at first should consist of milk (in Malta boiled); later, of broths and eggs and, if necessary, stimulants. Solids must not be freely given during high fever or when the tongue is coated. If appetite is present ordinary simple food may be taken. Lemonade or lime juice should be given after a time; not merely as a pleasant, thirst-relieving beverage, but with a view to averting scurvy—not at all an improbable complication if the diet is too restricted over a long period. Feeding must be conducted with the greatest circumspection, avoiding overfeeding on the one hand, and a low monotonous diet on the other. The tongue and the appetite are the best guides.

Exercise, travelling, and anything that tends to induce fatigue are prone to provoke relapse if indulged in prematurely; but a couch or chair in the garden is to be encouraged, weather permitting. The patient should rest for at least three weeks after temperature has become normal.

Flannel clothing should be worn, and frequently changed if there is much sweating.

Change of climate is not so necessary as in malarial affections, seeing that the disease may persist in England, and that it may gradually wear out in Malta. It is not desirable to move a patient when fever runs high, or when debility is very great, or

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when the cool and healthy season in the Mediterranean is at hand. It must be considered that at this time winter is approaching in England, with climatic conditions very unsuitable for a patient who has become anæmic and debilitated from a long course of fever; at this season he would do much better in Malta or Gibraltar. When, however, the case occurs early in the summer, or runs over the winter, then, in order to avoid the heat of the Mediterranean, change to England, if feasible and if it can be comfortably effected, should be advised.

When possible the subject of Mediterranean fever would do well to avoid the endemic area for one or more years after recovery.

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CHAPTER XX

TYPHOID FEVER IN THE TROPICS, AND TYPHO-MALARIAL FEVER

TYPHOID FEVER

The existence of typhoid fever in the tropics was for long not only ignored but actually denied, even by physicians and pathologists of repute. Formerly, the idea of malaria so dominated all views of tropical fevers that nearly every case of pyrexia, other than those of the most ephemeral description, or those associated with the exanthemata or with manifest inflammation, was relegated to this cause. When ulceration of the ileum was encountered *post-mortem*, the intestinal lesion was regarded, not as the specific lesion of the fever, but merely as a complication. More correct views prevail at the present day, and typhoid now ranks not only as a common disease in the tropics, but, to the European there, as one of the most commonly fatal. Little is known about typhoid as a disease of natives; Rogers has shown that in Calcutta, at all events, it is by no means uncommon among all classes. As a disease of Europeans it is only too familiar to the army surgeon in India and to the civil practitioner in most, if not in all, parts of the tropical world.

Besides being the scourge of the young European in India, typhoid is common enough in Japan, in China, in Cochin China, in the Philippines, in the Malay country, in Mauritius; the French have had large experience of it in Algeria and their West African possessions; the British have had similar experience in South Africa. It is also found in the West Indies; in Nigeria even; in fact, wherever it has been properly looked for.

Typhoid fever is, one might almost say, alarmingly

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prevalent among young soldiers and civilians in the East. It is very common among them during the first two or three years after their arrival. Fortunately, the liability decreases with length of residence. Apparently a sort of acclimatisation, or rather habituation, to the poison is established with time, just as tends to be the case with other organic poisons. It is not unlikely that the relative exemption—if such there be—of the native races is owing to a like immunising effect produced by living in constant contact with typhoid and similar toxic agents, or to an attack in childhood. On visiting native cities—Chinese cities, for example—one is filled with amazement at the state of filth in which the people live, and not only live but thrive. The streets are narrow and never cleansed; the common sewer lies beneath the flagstones, and through the interstices between the stones can be seen the black, stinking slush in the sewer. The sewage is not confined in a well-laid cemented drain, but it soaks through the loosely laid, uncemented stones, and thoroughly saturates the ground on which the tumble-down, overcrowded houses are built. Night soil is allowed to remain in wooden buckets inside the houses awaiting collection by the soil merchant, who sells it to the market gardener and the farmer. Urine is accumulated in earthenware jars, and is similarly disposed of. The houses are rarely swept and cleaned, hardly ever repaired. In every corner are filth and rubbish. And yet, in such circumstances—in which the sanitarian would prophesy typhus and typhoid—the population seems to thrive. Doubtless, where the European would almost surely contract typhoid and other filth diseases, the natives have obtained an immunity.

In Eastern countries little or no care is taken to prevent contamination of the wells and streams with sewage matter, and unless foreigners are very careful about boiling their drinking water and the water in which their dishes are washed, avoiding salads and other forms of uncooked vegetable dishes, avoiding bazaar-made drinks, and protecting their food and food dishes from flies and other mechanical trans-

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mitters of the *Bacillus typhosus*, they are almost sure, sooner or later, to fall victims.

It would appear that typhoid is not only a common disease among Europeans in the tropics, but that it is also a very virulent one, with a death-rate twice as heavy as the death-rate of typhoid in England. According to my experience in China, not only is the tropical form grave from the outset, but it is extremely liable to relapse. In England the death-rate is put down at about one in eight attacked; but in India the elaborate and carefully prepared statistics show a death-rate of rather over one in three. What with its frequency and its high rate of mortality, typhoid in India kills more European soldiers than does cholera.

Not only does typhoid exhibit increased virulence, but experience has shown that against it those sanitary safeguards which are found to be practically sufficient in England are by no means so effective in India. It would also appear that soldiers on the march contract the disease in passing through uninhabited country, in spite of the fact that the camp may be pitched in spots which, presumably, had never been occupied by man before, and although the men may have drunk only of water from springs and streams that were beyond suspicion of fæcal contamination. Similar testimony comes from Australia, where typhoid has occurred in the back country in lonely spots hundreds of miles from fixed human habitations. From these data the inference is suggested that Eberth's bacillus, under certain conditions of soil and temperature, may exist as a pure yet virulent saprophyte, for which an occasional passage through the human body is by no means necessary.

Anti-typhoid inoculation.—Having observed that injection into the subcutaneous tissues of the human subject of dead cultures of *Bacillus typhosus* conferred on the blood of the individual experimented on the power of agglutinating and sedimenting living cultures of the bacillus, Sir A. Wright, in the hope that in this circumstance he had grounds for concluding that protection against typhoid might be conferred

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by some system of artificial immunisation, devised such a system, and has practised it on a scale sufficiently extensive to warrant some conclusions.

During the Maidstone epidemic of typhoid in 1897, of 200 individuals, the subjects of special observation, 95 were inoculated, 105 were not inoculated. None of the former contracted typhoid, whereas 19 of the latter were attacked. Encouraged by these results, Wright proceeded to inoculate on a larger scale. In the *British Medical Journal* of January 20, 1900, he summarises his results up to that date. Of 11,295 British soldiers in India, to whom his observations apply, 2,835 were inoculated, 8,460 remained uninoculated. Of the former, 27 at some subsequent time had attacks of naturally acquired typhoid; of the latter, 213 were similarly attacked; the percentages being 0·95 and 2·5 respectively. In these attacks 5 of the previously inoculated died; 23 of the uninoculated. On the assumption that the whole of the British army in India was inoculated and that the foregoing results were maintained, there would be an annual saving of over 1,000 cases of enteric and of nearly 200 lives.

Since that time Sir A. Wright, with an industry and zeal in keeping with the important stake at issue, has steadily pursued his investigations. The English garrison in Egypt and the South African war afforded opportunities to test his conclusions in other fields, and on an extensive scale. The figures appear to justify the conclusion that these inoculations lead to at least a twofold reduction in the incidence of the disease in those inoculated, and a 50 per cent. reduction of the mortality. Crombie concluded from a careful and independent examination of the statistics, based on the results of inoculation as against non-inoculation in a group of 250 officers invalided from various causes from the South African war, that up to the age of thirty the advantage of a single inoculation is distinct—27 per cent. of the inoculated being attacked as against 51 per cent. of the non-inoculated. Beyond thirty he found the positions reversed, the advantage being with

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the non-inoculated. The results are better after a single than after a double inoculation, which appears, according to Crombie's figures, to increase the liability to infection.

Full details of the method of preparation and of the clinical effects of Sir A. Wright's inoculations will be found in the *Lancet* of September 19, 1896, and the *British Medical Journal* of January 20, 1900.

It is not requisite to enter further into the subject of typhoid fever, for although this important disease is abundantly common in the tropics, it is not properly classifiable as a tropical disease; moreover, it is fully dealt with in every text-book on general medicine. It is alluded to here rather by way of warning the practitioner in the tropics against overlooking it, and against assuming that every case of fever he may encounter is malarial; and, also, of indicating the special importance to him of a knowledge of the latest views in the practical value of anti-typhoid inoculation.

TYPHO-MALARIAL FEVER.

Some years ago a good deal was said, particularly in America, about "typho-malarial fever." An idea got abroad that there is a specific disease which, though resembling both, is neither typhoid, nor malarial, nor any of the other recognised forms of continued fever. There is no doubt that in warm climates, besides the known fevers, there are several, if not many, undifferentiated specific fevers But the clinical group indicated by the term "typho-malarial" is not one of these. Typho-malarial fever is an ordinary typhoid occurring in a person who has been exposed to malarial influences, *i.e.* who has become infected with the malaria parasite.

It has already been pointed out that the malaria germ may remain dormant for months or even years in the body, and then, on the occurrence of severe physiological strain—such as a chill, shock, excessive fatigue, and so forth—wake up again, and once more multiply and flourish in the blood and give rise to the

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phenomena of malarial fever. It is a recognised clinical fact, one familiar to our predecessors and much insisted on by them, that any disease process occurring in a person who has once had malarial fever is prone to take on an intermittent or periodic character; as if the previous malarial infection had left a sort of impress of periodicity on the constitution. Doubtless this is owing to the fact that in individuals with Laveran's parasite dormant in their tissues, the physiological strain implied by the presence of active disease paralyses for the time being the self-protective power, and the parasite is once more permitted to multiply and work its mischief in the blood. There are few more depressing influences than typhoid. Little wonder, then, that typhoid in a malarial is often accompanied by clinical evidences of a resuscitation of the malaria germ. And so it comes to pass that an attack of typhoid in malarial countries, or in persons returned from malarial countries, is prone to assume some of the characters of intermittent or remittent fever.

Not unfrequently, instead of the slowly increasing headache, malaise, creeping cold, anorexia, and day-by-day ladder-like rise of temperature, the first recognised sign of typhoid in such circumstances is a violent rigor, immediately followed by rapid rise of temperature, which, in an hour or two, mounts to 104° or 105°, to be succeeded in a few hours by profuse sweating and a partial remission of fever exactly resembling an attack of ague. For the next two or three days these attacks are repeated, the remission becoming less complete each time. Quinine may be given; but, although the rigors and marked oscillations of temperature are checked, the practitioner is surprised and disappointed to find that the temperature keeps permanently too high, and that the typhoid state is gradually developed. Or it may be that a typhoid fever begins in the usual insidious way, runs its usual course for a week or two, and then, in the middle of what is regarded as an ordinary typhoid, rigors and temperature oscillations and other malarial manifestations show themselves. If quinine is given these oscillations cease and the

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typhoid resumes its usual course. Or it may be that it is not until the end of the fever and during convalescence that these malarial symptoms are developed. Several such cases are now on record in which the malaria parasite was found in the blood.

The **diagnosis** between typhoid and some forms of malarial remittent is often exceedingly difficult, in certain cases almost impossible, without the assistance of the microscope and the serum test. The principal points to be kept in view are, first, the mode of incidence of the disease. In typhoid there is a gradual rise of temperature, a daily gain of a degree or so during several days, the maximum not being attained for five or six days; as against the sharp rigor and sudden rise of temperature through five or six degrees in the first few hours in malarial fever. Secondly, the characters of the gastric symptoms differ. Thus, in malarial remittent there is bilious vomiting and perhaps bilious diarrhœa, tenderness of the liver, epigastrium, and spleen, and an icteric tint of skin and scleræ; in contrast to the abdominal distension, perhaps the iliac tenderness and gurgling, and the peasoup stools of typhoid. Such signs as epistaxis, deafness, and cheek-flushing in typhoid have a certain weight, but skin eruptions in the tropics are of little aid in the diagnosis of such cases. Prickly heat, or its remains, is present in nearly everyone, sick and healthy, malarial or typhoid patient alike; so that rose spots are to be found in nearly all fevers in hot weather. None of these signs can be considered as absolutely diagnostic; all or any of them may be present in typhoid, and all or any of them may be present in malarial remittent. The only really diagnostic marks are tertian or quartan periodicity, amenability to quinine, and, above all, that supplied by the malaria parasite in the blood and the Widal serum test. In all doubtful cases the malaria parasite should be sought for; if it is found, the case has certainly a malarial element, and quinine is indicated. If it is not found, and if quinine has not been administered and several negative examinations of the blood have been made, and if the observer have confidence in his skill as a microscopist, the chances

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are the case is one of pure typhoid. Nevertheless, if the malaria parasite is found, typhoid is not necessarily excluded, for the case may be one of typhoid in a malarial, that is typho-malarial, fever.

No one who is proceeding to the tropics to practise medicine should fail to familiarise himself with the technique for the Widal reaction. In Europe he can fall back on the bacteriologist; in the tropics, as a rule, he cannot do this.

Prognosis and management.—Remittents under suitable treatment we expect to see recover; typhoids too often go the other way. A word of caution may be given as to prognosis and treatment. In forming diagnosis too much weight must not be attached to the presence or absence of diarrhœa; constipation is much more common in tropical typhoid than in the disease in Europe. Diagnosis, therefore, must not be too much influenced by absence of diarrhœa, and the practitioner must not be led by the presence of constipation into giving active purgatives. Purgatives are often of the greatest service in malarial remittent; but if, in consequence of a mistake in diagnosis, it is assumed that a case of typhoid is remittent, and large doses of calomel and other cathartics are administered, the result may be disastrous. If doubt exist about diagnosis, and quinine be given, it will not do a typhoid much harm. It is a good rule, therefore, when in doubt to give quinine, but to avoid purgatives.

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CHAPTER XXI

IMPERFECTLY DIFFERENTIATED FEVERS OF THE TROPICS

THERE can be little doubt that in the tropics there are a number of fevers specifically distinct from any of the foregoing, and also from the better-known fevers of temperate climates. Such fevers are constantly met with and are a perpetual puzzle to the conscientious diagnostician. Up to the present, little of a truly scientific character has been done towards describing, separating, and classifying them. Some attempts have been made to arrange these imperfectly differentiated fevers on a clinical basis; but, until their causes have been discovered and, above all, until they have been studied in reference to any possible connection they may have with the known pathogenic tropical parasites, anything like a sound classification and description has to be postponed. So far as known, they are not associated with distinctive exanthems or even with distinctive visceral lesions; a circumstance which has contributed, doubtless, to retard our knowledge in a very important department of tropical medicine.

The late Colonel Crombie, I.M.S., attempted a classification of these fevers on a clinical basis, which, so far as it goes, is of distinct value. His remarks apply solely to the fevers of India; but I can recognise in his descriptions clinical forms which I frequently met with formerly in China. It is fair to infer from this latter circumstance that, if these fevers are found in India and China, they probably occur also in other warm countries.

Crombie divided them into **simple continued fever, low fever,** and **non-malarial remittent.** To these I would add yet another, which, from experience in China, I regard as a distinct

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clinical entity, and which from its peculiar feature I would call **double continued fever.**

Since Crombie wrote, several observers have made important contributions to the subject, notably Thompstone and Bennett, who described under the name of hyperpyrexial fever what appears to be a special form of fever in West Africa; McCarrison, who has recently described a fever of three days' duration occurring in Chitral; and Rogers, who has still more recently described one of seven days' duration in Calcutta.

Simple continued fever.—Simple continued fever generally, if not invariably, commences with a rigor, the temperature rapidly or more slowly mounting to 104°, 105°, or even 106°. There is headache, malaise, a white furred tongue, anorexia, thirst, and perhaps vomiting. The fever lasts usually from three to eight days; occasionally it is prolonged for two, three, or four weeks. Crombie remarked that these cases are particularly common in towns, and were known locally as Bombay fever, Calcutta fever, and so forth. It might be suggested that such fevers are mild or aborted typhoid; but in the complete absence of the characteristics of enteric, the insignificant mortality, and the freedom from complications, so grave a diagnosis does not seem to be justified. It is customary to attribute them to heat, chills, change of season, acclimatisation, irregularities in diet, exposure to the sun, and the like. How far these ætiological speculations are correct it is hard to say.

Low fever.—Like the preceding, this type of fever is not an unusual one among Europeans in the tropics. Its characteristics are indefinite duration—weeks or months, a persistent though slight rise of temperature—rarely above 101·5° but never below 99°—anorexia, debility, loss of flesh, and a tendency to bilious diarrhœa. It is unrelieved by quinine or arsenic; but it almost invariably responds to a change of air, especially to a trip at sea.

Non-malarial remittent.—Crombie remarked that it is a pity we have no better name for this fever, which is of very frequent occurrence in India, and is

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one of the most fatal of the fevers there. Remittent is a misnomer, for the symptoms are even less remitting than those of typhoid. The temperature runs high, touching 104° or 105° for a long part of its course. It begins not unlike simple continued fever. By some it is considered a variety of typhoid, notwithstanding the absence of many of the symptoms of that disease. Hepatic enlargement and congestion are early and constant conditions; but the spleen, as a rule, is not distinctly enlarged.

"Bilious diarrhœa, in no respect resembling the diarrhœa of typhoid, is also a very frequent symptom. Quinine—often given in large and repeated doses in these cases—is not only not useful, but so obviously adds to the distress of the patient, without in any way producing an improvement in the progress of the symptoms, that it is very soon abandoned. Meanwhile, the temperature continuing persistently high, marked head symptoms, especially delirium of a muttering and irritable kind, come on, and the patient may even, and often does, pass into a condition of coma from which he can hardly be roused. This condition of persistent high temperature without marked remission, a distinctly enlarged and congested liver, bilious diarrhœa, congestion of the back of both lungs, and a low, muttering delirium, is generally reached by the eighteenth to the twenty-fourth day. If coma supervenes, the patient frequently dies about this period. In more favourable cases, where the symptoms are less severe, they may continue for a week or two longer. In such the average duration of the case is six weeks" (Crombie).

Crombie, although he had seen this fever in Europeans, regarded it as being essentially a disease of natives. It is seldom met with after the age of thirty, but is frequent enough in childhood.

Double continued fever.—In South China I encountered, both in Amoy and in Hong Kong, a peculiar type of fever, apparently of little gravity as affecting life, but sufficiently distressing while it lasted. Thorpe has recently recorded a case occurring in Wei-hei-wei. The disease is characterised

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by an initial pyrexial stage of from ten days' to a fortnight's duration, followed by a stage of from three to seven days' relative or absolute apyrexia, which, in its turn, is succeeded by another spell of about ten days' duration of smart fever, and then by convalescence (Fig. 56). Both in the primary and in the terminal fever the evening temperature may rise to 104° or 104·5°. It might be said that such cases are relapses of simple continued fever; but as I have seen, on at least two occasions, the same succession of events occurring almost simultaneously in two patients living in the same house —once in husband and wife, and once in brother and sister — it seems probable that this is a special form of disease, and that the double fever is a constant and characteristic feature. In the case of the brother and sister the march of their fevers was strictly simultaneous, the primary

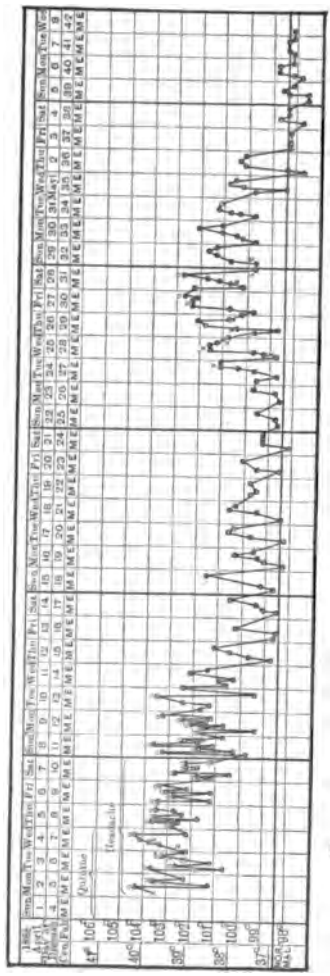

Fig. 56.—Chart of Double Continued Fever, Hong Kong. o indicates a dose of antipyrin.

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fever, the apyretic interval, and the terminal fever occurring in both patients on the same days. Beyond a certain amount of headache and febrile distress there are no special symptoms, so far as I have been able to observe, nor any special complications.

The three days' fever of Chitral.—*Definition.* — "An acute infectious disease, epidemic in the Chitral Valley during the summer months, and characterised by a single paroxysm of fever of typical course, which persists for about three days, without marked local affection. The paroxysm is accompanied by severe headache, pain in the back, bones, joints and muscles, and is followed by severe prostration, which continues for ten days or more after the attack."

Under the above title and definition McCarrison has described (*Ind. Med. Gaz.*, Jan., 1906) a well-defined type of fever annually prevalent in Chitral from April to July, and affecting more especially young natives and newcomers. So far, the disease has not been associated ætiologically with a micro-organism. Apparently it is not directly contagious, being acquirable in certain infected localities only; a circumstance suggestive of an animal intermediary.

In most instances one attack confers immunity, at all events during a current epidemic; second attacks occur in 5 per cent., and third attacks in 1 per cent. only. McCarrison brings forward evidence to show that, in the Chitral garrison, Europeans and Goorkhas were much more susceptible than Hindustanis. This relative immunity of the Hindoo he regards not as racial, but as having been acquired from previous attacks of the disease in the plains of India. If this be the correct interpretation of the relative freedom of the Hindustani in Chitral, we must conclude that three days' fever is common and endemic in India, and that it is more or less of an exotic in Chitral, where it can develop only when the atmospheric temperature reaches 75° F., or the temperature demanded by the animal intermediary (McCarrison suggests the sand-fly) subserving the germ. Possibly what used to be described and

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regarded as the fever of acclimatisation in India is this three days' fever.

Symptoms. — After an incubation period of from one to six days, with or without a prodromal stage, the fever is ushered in by slight or more severe rigor. The face becomes flushed, headache is intense, and there is usually severe general aching. In from 24 to 36 hours the temperature has reached 103°–4° F. It keeps about this point for a day longer, and then begins to fall, with or without epistaxis, vomiting, sweating or diarrhœa, reaching the normal about the end of the third or beginning of the fourth day. The patient continues debilitated, especially mentally, for a week or two longer.

Serious complications do not occur, but in some years diarrhœa, in other years pharyngitis, are features of the epidemic.

There are no important sequelæ. Desquamation is very rare; a point which, together with the absence of an eruption, serves to differentiate this fever from dengue, a disease resembling it in many respects. The mortality is nil in the healthy.

Treatment. — There is no specific known for this disease. Treatment must therefore be conducted on general principles.

As it would appear that three days' fever is a disease of locality, houses and places believed to be infected should be avoided, and, where possible, disinfected.

Hyperpyrexial fever.—From time to time we have accounts from the West Coast of Africa, where it is not uncommon in certain parts, of a peculiar type of fever, especially prevalent during the dry season, and which doubtless was formerly regarded and treated as malarial, but which, from the absence of the malaria parasite in the blood, and the impotence of quinine in checking it, we now know cannot be malarial. From its gradual incidence and prolonged course, although it is associated with hyperpyrexia, we know that it cannot be siriasis or heat apoplexy. What it may be is difficult to say; the probabilities seem to

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be in favour of its being a special form of tropical disease.

Symptoms.—Thompstone and Bennett describe the clinical features thus: "This fever is generally ushered in by a slight rise of temperature, followed by profuse perspiration and a fall in the temperature to about 99° F. After a period of apyrexia of perhaps twenty-four hours' duration, the temperature begins again to rise, slowly at first, but when 105° is passed, with alarming rapidity, one degree in ten minutes having been frequently observed, and it may reach 107° on the second day. For fourteen or even for thirty days subsequently there is absolutely no tendency for it to fall. The skin acts either very slightly or not at all, and all antipyretic drugs fail."

In due course the tongue becomes dry and shrivelled, but the spleen and liver are not enlarged; the urine is normal and abundant, the bowels being regular or loose. The conjunctivæ are injected, the pupils contracted. There is much anxiety and restlessness; but the mind is clear in most cases except when the temperature is very high.

If the patient is to recover, a change for the better may be looked for about the end of the third week. Convalescence is very gradual, and it may be six weeks before temperature is normal. Half the cases die.

A curious feature is the remarkable rapidity with which the blood coagulates the moment it is exposed to the air.

Malaria parasites, though carefully sought for, have not been found; neither have any attempts at cultivations from the blood yielded any micro-organism. The white corpuscles are rather in excess.

Treatment.—The only treatment which has been of value is the diligent use of the cold bath and the cold pack.

Seven Days' Fever of Indian Ports.—*Definition.* — A short fever occurring epidemically during the summer months in Indian ports and characterised by sudden invasion, severe headache, pains in the back and limbs, and pyrexia of a

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peculiar saddle-back type—occasionally of a continued type—lasting from six to seven days and associated with a pulse which is relatively slow in comparison to temperature.

History.—Possibly this fever is one of several fevers included under the somewhat comprehensive term, simple continued fever. Rogers, by a careful study of a vast number of cases of fever in Calcutta, observing that this particular type has a definite seasonal incidence during the late hot weather and the early monsoon months in Calcutta, and declines just at the time when the principal malarial rise of the year takes place, concludes from this and from the absence of malarial parasites that it cannot be malarial, from the absence of respiratory symptoms that it is not influenza, and from the absence of violent joint pains and eruption that it cannot be dengue. He cultivated a bacillus from the blood, but did not succeed in establishing any causal relationship of the organism to the disease. He further states that it usually begins amongst the sailors and spreads later to the townpeople; that it occurs in other Indian ports, but is probably unknown in the interior of the country. Apparently it is a mild disease, has no mortality, and no distinctive pathological anatomy.

Diagnosis.—The diagnosis of these imperfectly differentiated fevers is always a difficult matter, specially so during their early stages. Among other possibilities that of typhoid, of undulant (Mediterranean) fever, malaria, of kala-azar, dengue, influenza, and other infections has to be considered. The persistent absence from the blood of the malaria parasite and of pigmented leucocytes, if vouched for by an experienced observer, and the negative results attending administration of quinine, together with the absence of definite periodicity in the symptoms, of pronounced anæmia and of marked enlargement of the spleen, should be decisive against malaria. But, in the present state of our knowledge, it is very hard indeed to exclude typhoid, paratyphoid

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and undulant fever until the case is well advanced. It may be that further experience of the blood serum tests will establish their title to be regarded as absolutely pathognomonic signs. In this event the practitioner will have in his possession an invaluable aid in the diagnosis of tropical fevers. As things are at present, in cases in which there is the slightest doubt it is an excellent rule to regard all doubtful fevers as being possibly typhoid.

Treatment.—It is well at the commencement of doubtful tropical fevers to be as guarded in treatment as in diagnosis, and to eschew active purgatives, to enjoin rest in bed, to place the patient on a bland, unstimulating fluid diet, and to confine medication to some innocent fever mixture. There is no specific treatment for any of these imperfectly differentiated fevers. Each case has to be dealt with on its own merits and on general principles. Headache may be relieved by cold applications to the forehead, by an ice cap, or, especially if temperature rises high, by sponging and, if not otherwise contra-indicated, by occasional doses of phenacetin or some similar drug. If quinine, on the supposition that the case is malarial, has been freely tried, and without benefit, it must not be persisted with. As already hinted, "low fever" should be treated by change of air, and more especially, where feasible, by a trip to sea.

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CHAPTER XXII

PELLAGRA

Synonyms. — Pellarella, Alpine scurvy, Asturian leprosy, Asturian rose, disease of the Landes, dermotagra.

Definition.—An endemic disease of slow evolution, characterised by a complexity of nervous, gastric and cutaneous symptoms, which make their first appearance during the spring months, and recur year after year at the same season, remitting more or less during the winter months. It is confined almost exclusively to field labourers, and the more distinctive features are—(*a*) a remitting erythema of the exposed parts of the body; (*b*) marked emaciation; (*c*) profound melancholia alternating with mania.

Geographical distribution. — *Europe:* Pellagra has a wide distribution in Southern Europe. It is found in Northern Portugal, in Spain, in Italy, in the south-west of France, in the Austrian Tyrol, in Hungary, Croatia, Dalmatia, Bosnia, Servia, Bulgaria, Turkey, Greece, Corfu, Roumania, Bessarabia, Kherson, and Poland. *Africa:* Algeria, Tunis, Egypt, the Red Sea coast, and amongst the Kaffirs and Zulus. Sandwith found it in 1900 among the coloured lunatics on Robben Island. *Asia:* Information is scanty, but it has been reported from Asia Minor and North Behar in India (Ray, 1902). *America:* Mexico, Brazil, the Argentine, Barbados, and probably in other West Indian islands. *Australasia:* Neirte has reported it in New Caledonia.

History.—The history of pellagra is comparatively recent. The disease was recognised and described almost simultaneously in Italy and Spain. In Spain it was first described by Casal in 1762 under the name of *Mal de la Rosa*, but he stated that the disease had been endemic in Oviedo since 1735, although unknown in other parts of the Asturias. Subse-

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quently it became widely diffused throughout the Iberian peninsula. In Italy the disease, under the name of Alpine scurvy, was described by Odoardi in 1776, but it had been recognised previously by Pujati in 1740. Ramazzini, in 1700, writes of a disease under the name of *Mal del Padrone*, which appears to have been pellagra. Frapolli, who described the disease in 1771, under the name of pellagra, says that probably it is the same as pellarella, a disorder mentioned as early as 1578 in the rules of admission to the Ospedale Maggiore in Milan. Pellagra appeared first in the provinces of Lombardy and Venice. By the end of the eighteenth century it had spread over the greater part of Northern and Middle Italy. Quite recently it has appeared in the Southern Provinces, in Sardinia and Sicily, regions previously immune.

The earliest mention of pellagra in France dates from 1829, when Hameau published an account of cases observed since 1818 around Teste-de-Buche and in the plain of Arcachon. He describes its subsequent spread in the coast region of the Gironde.

In Roumania the first appearance of the disease is assigned to the year 1833; in Corfu to 1839.

We know nothing of the history of pellagra in Egypt. The first mention of its existence there is in Pruner's "Topographie medicale du Caire," published in 1847. Pruner's statements were discredited by Hirsch and others, but recently Sandwith has shown that the disease is very prevalent in Lower Egypt, and also, though to a less extent, in Upper Egypt.

Ætiology.—*Sex.*—Both sexes are liable; as a rule the disease is more prevalent in men. The degree of prevalence amongst women varies greatly in different places, apparently according to the share they take in field work.

Age.—As already stated, pellagra is chiefly a disease of middle age, the majority of cases occurring between 20 and 50. Infants are very rarely attacked.

Occupation.—The disease is almost confined to field labourers. The inhabitants of towns, even of those in the very heart of intensely pellagrous districts, enjoy an immunity similar to that of town-inhabitants as regards malaria. Felix points out that pellagra is quite exceptional amongst the Jews, who, as a race, rarely engage in agriculture. Bouchard says that herdsmen in pellagra regions are exempt.

Season.—The disease first shows itself in the spring months (February, March, April), and its

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relapses take place year after year at the same season. Occasionally relapses may occur in autumn.

Topographical distribution.—The scanty information we have as to the topographical distribution of pellagra seems to show that the disease is limited principally to low districts and to such places as have a high ground-water level.

Epidemiology.—Pellagra is regarded as being strictly endemic, but everywhere it has shown a marked tendency to slow extension. Thus still very common in the north of Italy where it first appeared, pellagra in recent years has become increasingly prevalent in Umbria and in the Marche, and has extended to the provinces of Siena and Grosseto in Tuscany, those of Campobasso, Teramo and Aquila in the Abruzzi and Molise, the province of Rome, the Campagna, the Puglie, Sicily and Sardinia. When once established in a district it remains there, but the degree of prevalence varies considerably from year to year, and not always in direct ratio to the amount of rainfall or the hygrometric state of the atmosphere, as has been asserted. In proportion as the area of pellagra has extended, the number of cases in the original seats of the disease has usually increased. Thus the number of pellagra patients in Lombardy in 1839 was 20,282; in 1856 it had risen to 38,777; in 1879 to 40,838; in 1881 it had reached 56,000.

The virus.—Pellagra has been ascribed to the most varied causes, such as insolation, poverty, insanitary dwellings, syphilis, irritant oils, bad water, alcohol, garlic, onions, maize. Some have regarded it as a modified or degenerate form of leprosy, others as "sunstroke of the skin," and D'Oleggio, in 1784, proposed that it should be called "vernal insolation." "Sun disease" was an old popular name, and certainly the skin manifestations of pellagra are influenced by the action of the direct rays of the sun. This was proved experimentally, first by Gherardini, who varied the limits of the eruption by systematically displacing parts of the clothing; and later by Hameau, who obtained differently shaped patches of

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erythema by means of gloves fenestrated in different ways. In small-pox and also in other exanthemata we notice a decided influence of light, more particularly of the actinic rays, on the production of their skin eruptions. Although light may influence the eruption in pellagra, this is no adequate reason for concluding that insolation is the cause of the disease, any more than that it is the cause of small-pox. The eruption being limited to the spring season and lasting about a fortnight only disproves the insolation theory.

It would be idle to discuss the arguments brought forward to show that pellagra is caused by bad water, insanitary dwellings, poverty, syphilis, leprosy, alcohol, oil, onions, or garlic. The maize theory, on the other hand demands, because of its popularity, a searching scrutiny.

The general opinion is that pellagra appeared soon after the introduction of maize into Europe, and that it advanced *pari passu* with the extension of maize cultivation, and with the more general adoption of the new cereal as an article of food. For these and other reasons maize is held to be the causative agent of pellagra, as rice has been held to be the cause of beriberi; and, just as in the latter case, various theories have been advanced to explain the operation of the assumed cause.

The morbific action of maize has been variously attributed to—

(*a*) Deficiency in its nutritive principles.

(*b*) Specific toxic substance contained normally in the grain.

(*c*) Poisons elaborated after it has been ingested.

(*d*) Toxic substances elaborated during decomposition of the grain.

(*e*) Fungi or bacteria found on maize.

(*a*) *Deficiency in nutritive principles.*—Maize stands high as regards alimentary value. Insufficient nourishment may bring about inanition and marasmus, but never causes specific lesions like those of pellagra. Entire populations who live solely on rice or potatoes remain quite free from this disease, although these foods are far inferior to maize in nutritive value.

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(*b*) *Specific toxic substances normal to maize.*—Those who advanced this theory were obliged to stipulate for a special personal susceptibility, otherwise the immunity of the millions who live on Indian corn could not be accounted for.

(*c*) *Poisons elaborated from maize within the alimentary canal.*—Neusser regards pellagra as a peculiar form of autointoxication. A similar theory was propounded by De Giaxa in 1903. The latter ascribes the disease to a poison resulting from the action of *Bacillus coli* on sound maize after ingestion. He claims to have produced the anatomical lesions of pellagra in dogs by feeding them on porridge made with sound maize, and also to have obtained the same symptoms and lesions in animals inoculated with a toxin produced *in vitro* by the cultivation of *Bacillus coli* in maize media. These theories are disposed of by the harmlessness of maize in non-pellagrous districts.

(*d*) *Toxic substances elaborated in decomposing maize.*—Lombroso, in 1871, claimed that pellagra is due to the ingestion of certain toxic substances elaborated by saprophytes acting on the grain. In conjunction with others, he obtained from fermenting maize a watery extract containing a narcotic principle resembling conin, and also an alcoholic extract and a red oil, both containing an alkaloid resembling strychnine, "pellagrozein." These two toxins combined, he holds, give rise to pellagra in the same way as sphacelinic acid and cornutin are believed to give rise to ergotism. In fowls inoculated with the toxins, Lombroso observed diarrhœa, loss of feathers, and death; in rats, wasting, choreiform movements, muscular spasm, and death; in men, vomiting, diarrhœa, desquamation of the epidermis, giddiness, dilatation of the pupil, and malnutrition.

These acute symptoms are in no way comparable to pellagra; identical results follow the administration or inoculation of analogous substances prepared by similar methods from wheat and other harmless foods.

Different investigators have extracted from damaged maize very different substances. Hausemann found a narcotic tetanic poison which he called "maizina." Selmi demonstrated the presence of ammoniacal acrolein. Pellogio extracted a bitter substance which produced paralytic symptoms. In 1881, Monselice analysed various specimens of damaged maize collected in pellagra districts, but was unable to find any alkaloid. He pertinently remarks that artificially fermented maize and the ordinary damaged maize are two very different things. In 1894 Pelizzi and Tirelli made experiments on dogs and rabbits, administering *per orem*, or injecting subcutaneously or endovenously the toxic substances obtained from cultures of the bacteria of maize. They observed spastic paresis of the posterior limbs and other symptoms which they considered characteristic of pellagra. Gosio, having observed that the commonest saprophyte of maize is *Penicillium glaucum*, prepared pure cultures of this fungus and extracted a substance belonging to the aromatic series. Ferrati made some experiments

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with a tincture of penicillium-damaged maize, and found that it is exceedingly toxic to rats, the animals dying in a few hours. Di Pietro noticed that only a certain variety of *Penicillium glaucum* has toxic properties. The poisonous substance is not present in cultures before the third day; it is a glucoside, and is found in the spores only. Experiments on guinea-pigs, dogs, cats and rabbits, produced symptoms very different from those obtained by Lombroso and others, but Di Pietro considered them characteristic of pellagra. Di Pietro also tested the toxic properties of *Penicillium glaucum* on himself, and suffered from pyrosis, vomiting, giddiness, weakness in the legs, slight tremor of the arms, frequent micturition. Lastly, in 1904, Fossati declared he induced pellagra by feeding or inoculating guinea-pigs with maize damaged either by *Aspergillus fumigatus* or *Penicillium glaucum*. These results are mutually contradictory.

(*e*) *Micro-organisms found on maize.* –Ballardini, in 1845, was the first to attribute pellagra to a living organism, a mould (*Sporisorium maydis*), which he found in the greenish stain (*verderame*) frequently seen in the germ-groove of maize grains. Experiments gave rise to gastritis and diarrhœa in man, loss of feathers and general wasting in fowls. Lombroso pointed out that *Sporisorium maydis*, on account of its rarity, could not be the cause of pellagra, and that Ballardini had probably confounded the *Sporisorium* with *Penicillium glaucum*. A special commission reported against Ballardini's discovery, on the ground that the *verderame* was common in many non-pellagrous districts of Italy. However, notwithstanding this, Ballardini's theory was accepted by many in Italy, and by Roussell and Costallat in France.

In 1860, Pari incriminated the maize smut (*Ustilago maydis*), pointing out that the spores of this fungus are invariably present in the dust of the hovels of the peasants, who store their maize in the rooms in which they sleep. Generali fed two horses on fodder mixed with the maize smut, and claimed that after seven months one of the animals presented a skin eruption on the parts most exposed to the sun. But Professor Imhof, who made some experiments on himself, proved that the maize smut is harmless to man.

In 1881, Majocchi found in both normal and diseased maize a very motile micro-organism which he named *Bacterium maydis*. He claimed to have found this organism in the blood, brain, liver, heart, kidneys, lungs, intestinal mucosa, and erythematous skin of pellagra patients, and on these grounds brought it forward as the causative agent of the disease. Cuboni found a similar bacillus in damaged maize, and in the stools of pellagra patients. Paltauf, who investigated pellagra, in 1889, on behalf of the Austrian Government, examined fifteen patients, but found Cuboni's bacterium in the stools of one only. However, he found it to be a very common saprophyte of damaged maize, and, together with Heider, proved that the maize toxins were partly due to the metabolic

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action of this organism. At the same time he showed that *Bacterium maydis* is no other than the well-known potato bacillus (*Bacillus solanacearum*) and that its toxic effects do not resemble pellagra.

In 1896 Carrarioli also claimed to have found a bacillus in the blood, saliva, and stools of pellagra patients. He stated that he had inoculated the toxic products of this organism subcutaneously into various animals, and that he also had invariably obtained symptoms similar to those of pellagra. He went so far as to name the organism *Bacillus pellagræ*.

In 1902 Ceni stated pellagra to be a true mycosis due to two different species of *Aspergillus*, *A. fumigatus* and *A. flavescens*. He declared that the season in which pellagra symptoms appear in man corresponds to "the cycle of annual biological evolution" of these hyphomycetes. Moreover, he stated that he had been able to isolate almost constantly, and usually in pure culture, the two Aspergilli from the lungs, pleura, pericardium, and meninges of pellagra cadavers, and, further, that the spores of the fungi pass through the intestinal wall and thus reach the other organs.

In a later work Ceni, together with Besta, ascribes pellagra not to the organisms themselves, but to elaborated toxins. More recently Ceni and Besta describe two special varieties of *Penicillium glaucum* as the true cause. According to these authors the toxic properties of one variety are excitative and therefore cause the acute forms of the disease; those of the other, being narcotic, give rise to a more chronic type. Tiraboschi, who has recently (1905) made a very careful study of the hyphomycetes found on maize grains in pellagra districts, states that he never found *A. flavescens*, and believes that Ceni and Besta must have confounded it with *Aspergillus varians*, which is very common. He also states that *A. fumigatus* is rare, while Ceni and Besta stated that both *A. flavescens* and *A. fumigatus* are very common, and in some seasons even more common than *Penicillium glaucum*.

The fungus incriminated by the majority of authors as the causative agent of pellagra is, strange to say, the common blue mould, *Penicillium crustaceum* (*P. glaucum*), which is found everywhere and on the most heterogeneous media.

In contemplating the fungus theory of pellagra it is interesting to note that of all the diseases known to be caused by fungi, such as thrush, ringworm, pinta, tinea imbricata, mycetoma, actinomycosis, pneumonicosis, not one in any way resembles pellagra.

In examining the numerous observations that have been made, there is one fact which stands out very prominently, and that is that each investigator claims to have reproduced true pellagra either in animals or man, sometimes in himself, by inoculating beneath the skin, injecting into the veins, or adminis-

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tering *per orem* the special organism or toxic product which he happens to have isolated. But the peculiar symptoms and anatomical lesions of pellagra, together with its epidemiology, seasonal habit, and geographical distribution, show very clearly that the disease must have one specific cause and cannot be brought about by each, or all, or any of the numerous aforementioned fungi, bacteria, and chemical products. It would be unwise, therefore, to place much reliance on these experiments. The interpretation of experiments is often as fallacious as the interpretation of ordinary natural facts. The history of the investigation of almost every disease furnishes examples in plenty. Richardson claimed to have produced genuine rheumatism by injecting or administering *per orem* lactic acid; Klebs and Tommasi Crudeli, typical malaria in animals by inoculating a bacillus found in the soil of malarious localities; Sanarelli, yellow fever by inoculation of *Bacillus icteroides*, and so on.

The maize theory of pellagra is based chiefly on the belief that the disease appeared soon after the introduction of maize into Europe, and that it everywhere followed the extension of maize cultivation, and increased with the more general adoption of the new cereal as an article of food. This opinion has been repeated by almost every writer on pellagra. Neither the statement nor the argument is indisputable. In the first place we know nothing positive about the introduction of maize into Europe. The general belief is that it was brought over by the Spaniards from South America; on the other hand there is historical evidence that maize was cultivated in the old world hundreds of years before the discovery of America. Although we have no positive information as to the date of its introduction into Italy, it is certain that maize was used there as an article of food about the middle of the sixteenth century, that is to say, about 200 years before the date assigned to the appearance of pellagra. We are thus confronted by a very serious dilemma, for if we allow that pellagra existed and was known, it may be under other names, previous to its

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recognition by Frapolli in 1771, then we can no longer assign a date for its introduction into Italy, and thus the most powerful argument in favour of its association with maize is lost. If, on the other hand, we maintain that pellagra did not exist in Italy prior to that date, then it is difficult to explain why it did not show itself soon after the introduction of the incriminated cereal.

It has been pointed out again and again by numerous observers that the areas of pellagra endemicity and those of maize culture do not correspond; indeed, there are vast regions in which maize is extensively cultivated and much eaten, but in which pellagra is absolutely unknown. A most convincing example is that of the United States of America. On the other hand, pellagra has been observed very frequently in places in France, Spain, and Italy in which maize is not cultivated and in people who have never used it as an article of food. To overcome these embarrassing facts, so telling against the maize theory, the comfortable term "pseudopellagra" was invented. The disease is pellagra when it fits in with the orthodox theory and when it can be connected in any way with maize; but when this is not possible, the disease becomes a "pseudopellagra"!

A comparative study of the distribution and prevalence of pellagra at different periods is decidedly unfavourable to the maize theory. In the days of Casal, the Province of Oviedo in Spain was one of its chief centres. In 1900 this was the province which suffered least, the highest incidence of the disease being in the Province of Madrid. Now, no change whatsoever has taken place in the maize cultivation of the Province of Oviedo; the people eat maize there to-day just as freely as they did in Casal's time, and there has been no improvement in the storage or preparation of the grain. On the other hand, maize is hardly ever used as an article of food in the Province of Madrid.

After pointing out (*British Medical Journal*,

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1905) how unsatisfactory are the prevailing theories as to the causation of pellagra, Sambon suggests that it probably belongs to the protozoal group of diseases. He states that pellagra shows many analogies with such diseases as syphilis, trypanosomiasis, and kala-azar. In pellagra, as in trypanosomiasis, we find the same characteristic perivascular small cell infiltration. In both diseases arsenical treatment appears to be beneficial. The mononuclear increase in the blood of pellagra patients is an additional argument in favour of the suggestion.

Symptoms.—Pellagra usually begins with feelings of weakness and a consequent disinclination to work. The patient is pale, has a peculiar staring look, and complains of headache, giddiness, and vague but often severe pains in the back and joints. His character changes. He becomes irritable, and at the same time stupid and morose.

At first the tongue is coated; later it loses its epithelium, the denudation extending not infrequently to the palate and gullet, and giving rise to a sore condition, accompanied by a saltish taste and copious salivation. The gums may be swollen and bleed easily, a condition which gave rise to the name "Alpine scurvy." There may be eructations of gas, nausea, and vomiting. The appetite is variable. The epigastric region, and sometimes the lower part of the abdomen, are tense and painful. Constipation is usually present, but in some instances there is diarrhœa, and the stools may contain blood.

From the commencement an erythema, not unlike a severe sunburn, is observable on those parts of the body which are, as a rule, unclothed and exposed to the sun. The eruption is characteristic. It appears suddenly, first on the back of the hands and feet, then on the forearms, legs, chest, neck, and face. The patches of erythema are irregular in outline and intensity. The affected area is swollen and tense, and is the seat of burning or itching sensations, which become particularly acute on exposure to the sun. The congestion disappears completely, but

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temporarily, on pressure. Petechiæ are common on the affected parts, and blebs may form with clear, opaque or blood-stained contents of feebly alkaline reaction. The eruption usually lasts about a fortnight, and is followed by desquamation, which leaves the skin rough, thickened, and permanently stained of a light sepia colour. It is on account of this roughness of the affected skin that the disease is called "pellagra," an Italian word meaning rough skin.

Implication of the nervous system is indicated by tremor of the tongue, exaggerated deep reflexes, and mid-dorsal spinal tenderness. The patient suffers from obstinate sleeplessness, occasionally from uncontrollable sleepiness. He experiences great weakness, especially in the lower extremities, and is subject to peculiar attacks of giddiness, with a tendency to fall forwards or backwards. Another characteristic symptom is a feeling of burning in the palms of the hands and the soles of the feet.

As a rule there is no marked permanent elevation of temperature, but periods of slight fever occur irregularly.

Two or three months after onset symptoms abate and, although the skin remains dark-coloured and rough, the disease appears to have come to an end. Next spring, however, the whole series of phenomena recurs in a more severe form. The eruption assumes a darker colour. The depression of spirits deepens into melancholia, which may have maniacal interludes, with a peculiar tendency to suicide, especially by drowning. The general feeling of weakness increases, the patient loses weight and is unable to work; his gait becomes uncertain and somewhat of the spastic paraplegic type. The pains in the head and back become very acute, and there may be lightning pains, cramp, twitchings, tremors, and even epileptiform seizures of the cortical variety.

For several years the disease may thus recur in the spring with increasing severity. The patient becomes greatly emaciated, paralytic, and completely demented. Helpless, bedridden, suffering from incontinence of urine and uncontrollable diarrhœa, covered

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with bed sores and neglected, he dies from exhaustion or from some intercurrent disease.

The duration of pellagra is exceedingly variable. It may last only two or three years; it usually extends to ten, fifteen, or more.

Cases differ considerably. In some the nervous symptoms predominate, in others the gastro-intestinal, in others again the cutaneous. Forms of hyperæsthesia may occur in different regions of the body. Ocular symptoms, such as ptosis, hemeralopia, diplopia, amblyopia, mydriasis, are not uncommon. The urine is generally alkaline, and may rapidly become ammoniacal. It may contain tube casts and traces of albumin. The erythrocytes and hæmoglobin are diminished. Sambon and Terni in Italy, Grigorescu and Galasescu in Roumania have noticed a relative increase of the mononuclear leucocytes, a point differentiating the eruption of pellagra from ordinary erythemas.

A very acute form has been described under the name of "pellagra typhus." In this there is intense prostration, high temperature, delirium, trismus, stiffness of the neck, and sometimes opisthotonos. This pellagra typhus may be ordinary pellagra complicated with other diseases, such as enteric, cerebro-spinal or malarial fever.

Morbid anatomy.—The pathological features essential to pellagra are usually obscured by complicating diseases.

A constant and striking feature is the great emaciation. The viscera show chronic degenerative changes, particularly fatty degeneration and a characteristic deep pigmentation. The intestinal walls are greatly attenuated through wasting of their muscular coat, while at the same time the mucous lining is hyperæmic and, not infrequently, ulcerated. The liver and spleen are usually atrophied.

The brain and cord lesions consist of a chronic leptomeningitis, often with much thickening, and even with the formation of osseous plaques. The principal and essential changes are a perivascular cell-infiltration, similar to that of trypanosomiasis, and pigmentation

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and degeneration of the nervous elements. There may be actual wasting of the brain, and the ventricles may be distended by an excess of fluid. In the cord the lateral columns and the crossed pyramidal tract are especially implicated, but the direct cerebellar tracts usually escape. The anterior cornual cells are frequently atrophied and deeply pigmented. The posterior columns do not escape, the median portion being often degenerated. The degenerative changes in the lateral columns are chiefly in the middle and lower third of the dorsal region, those of the posterior columns principally in the cervical and upper dorsal region. The disease, clinically and anatomically, presents much resemblance to general paralysis of the insane.

Diagnosis.—Of course, doubtful cases are occasionally encountered, but a localised erythema associated with nervous symptoms, particularly mental symptoms, great debility and seasonal recurrence, in a person in or coming from a pellagrous district, can hardly be confounded with any other disease. Once seen, pellagra is easily recognised again.

Treatment.—Lombroso recommends the administration of arsenic, and states that it has proved most beneficial. A special serumtherapy has been attempted, but so far without success. Many of the milder cases seem to recover when removed from the endemic area and placed under good hygienic conditions. In its advanced stage the disease is practically incurable. In Italy the government, basing its action on the maize theory of pellagra, has provided drying apparatus for grain bakeries, and other hygienic advantages, including better house accommodation, also special asylums (*pellagrosari*) for the treatment of the disease in its earlier stages. It is stated that a decrease of the malady has followed these measures. Notwithstanding, pellagra seems to have increased of late years, especially round Perugia and in other districts of Northern Italy in which these measures have been most strictly carried out.

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CHAPTER XXIII

HEAT-STROKE

THE term "heat-stroke" conveys the suggestion that heat is the leading ætiological factor in the various morbid conditions which custom has grouped under this and similar names.

Until irrefutable evidence has clearly demonstrated the true cause of any given disease, it is a very grave error to base the name of such disease on some crude hypothetical ætiological conception. Such a nomenclature is sure to lead to confusion, to mistakes in practice, and to retard progress. There is no better illustration of the truth of this remark than that supplied by the group of diseases under consideration.

The expression "heat-stroke" covers several distinct, one might say of two of them almost opposite, clinical conditions. One of these is *heat-exhaustion*, virtually a syncope, which may occur anywhere and in any climate, high atmospheric temperature, whether natural or artificial, being its essential ætiological factor. The other, of which hyperpyrexia is the most striking clinical feature, is a well-defined and possibly specific fever, having a peculiar endemicity and assuming at times in the endemic area almost epidemic characters. Like yellow fever, dengue, tropical elephantiasis, and other tropical diseases, this second form of heat-stroke occurs only in conditions of high atmospheric temperature; but, as with these diseases, it by no means follows that, though occurring *in* high temperature, it is caused *by* high temperature. To obviate confusion, and following the example of Sambon, I shall describe this disease under its ancient name *Siriasis*.

Besides these two well-defined morbid states associated with high atmospheric temperatures there is another, but ill-defined group of heat-stroke cases

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which, to all appearance, result exclusively from exposure to the direct rays of the sun. These cases might be classified under the term *Sun-traumatism.*

Although not all of them strictly classifiable as fevers, in deference to custom and for convenience I shall describe these three phases of so-called "heat-stroke" in this place and as a group.

HEAT-EXHAUSTION.

Definition.—Sudden faintness, or fainting, brought about by exposure to high atmospheric temperature.

Ætiology.—The healthy human body, when untrammelled by unsuitable clothing, when not exhausted by fatigue or excesses, when not clogged by surfeit of food, by alcoholic drinks or by drugs, can support with impunity very high atmospheric temperatures. In many parts of the world men live and work out of doors in temperatures of 100° or even of 120°. Many industries are carried on at temperatures far above this; glass-blowing, sugar-boiling, for example. The stokers of steamers, especially in the tropics, discharge for hours their arduous duties in a temperature often over 150° F.

When, however, the physiological activities have become impaired by disease, especially by heart disease, kidney, liver, or brain disease, by malaria, by alcoholic or other excesses, by fatigue, by living in overcrowded rooms; or when the body is oppressed by unsuitable clothing; or in the presence of a combination of some of these, then high atmospheric temperatures are badly supported, the innervation of the heart may fail, and syncope may ensue. Chevers, than whom few have had better opportunities of forming a sound opinion, speaking of this subject, says: "Numerous as the constitutional causes of heat-strokes are, all Indian experience combines to show that drunkenness is the chief." The tropical practitioner will do well to bear this remark in mind; it applies not only to heat-exhaustion, but also to all forms of disease grouped under the term "heat-stroke."

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Heat-exhaustion, then, is one form of what, when the subject of it happens at the time to be exposed to the sun, is called "sun-stroke," or when the patient happens to be at the time under cover is called "heat-stroke." In nine cases out of ten this sun-stroke, or heat-stroke, simply means syncope; syncope caused by solar or atmospheric heat, or a combination of these, acting on a body whose resistance has been impaired by disease, or by trying, unphysiological conditions. This form of heat-stroke, consequently, has no special geographical distribution and no special morbid anatomy or pathology. For obvious reasons it is most apt to occur in warm weather, and in tropical climates; and on this account its recognition, prevention, and treatment have special claims on the students of tropical medicine.

Symptoms.—When attacked with heat exhaustion the patient feels giddy, and perhaps staggers and falls. He is pale; his pulse is small, soft, and perhaps fluttering; his breathing is shallow, perhaps sighing, never stertorous; his pupils are dilated; his skin is cold; his temperature is subnormal; and he may be partially, more rarely wholly, unconscious. Usually after a short time he gradually recovers; very likely with a splitting headache and feelings of prostration. In a small proportion of cases the faint is not recovered from, and death ensues.

Treatment.—In syncopal heat-stroke the patient should be laid at once on his back in a cool, airy, and shaded place. His clothes should be loosened, a little water dashed on his face and chest, and ammonia held to his nostrils. If necessary, a stimulant may be given by the mouth, or injected into the rectum or hypodermically. It is a mistake to douche these cases too freely. The object is rather to stimulate than to depress.

SIRIASIS.

Definition.—An acute disease developing in the presence of high atmospheric temperature, and characterised by sudden incidence of hyperpyrexia, coma, and extreme pulmonary congestion.

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Nomenclature.—This is, perhaps, the most important of the several diseases covered by those loosely used terms—sun-stroke, heat-stroke, *coup de soleil*, insolation, heat-apoplexy, heat-asphyxia, thermic fever, and so forth. I adopt the name siriasis because, whilst distinctive, it embodies no ætiological theory; it has the further merit of being the most ancient of the many names applied to the disease.

The **geographical distribution** of siriasis appears to be remarkably restricted. It is true that this type, or what passes for this type, of disease has been reported as occurring in many countries. On careful examination it will be found that a large proportion of the reputed cases are really examples of other diseases, more especially of cerebro-spinal fever, apoplexy, tubercular meningitis, delirium tremens, pernicious malaria, or some other phase of acute disease, but not of true siriasis. According to Sambon, hyperpyrexial heat-stroke is rigidly confined to certain low-lying, sea-coast districts, and to the valleys of certain rivers. It is never found in high lands, nor above a relatively low altitude—600 feet.

It is unknown in Europe. The endemic areas are—in America, the east coast littoral of the United States, more especially in the great towns, the Mississippi valley, the coast of the Gulf of Mexico, the valleys of the Amazon and of the La Plata, and the South Atlantic coast; in Africa, the valley of the Nile, the coasts of the Red Sea, and a low-lying part of Algeria near Biskra; in Asia, Syria, the valleys of the Indus and Ganges, Lower Burma, Tonquin, and south-east China; in Australia, the Murray River district, the Queensland coast, and, possibly, the plains of Sydney. No doubt it occurs elsewhere in corresponding meteorological and telluric conditions; but, undoubtedly, many large areas in the tropical world, and especially so the interior of continents, are exempt from siriasis. It is not met with on the high seas, although it is well known on ships in the narrow, land-locked Red Sea and Persian Gulf.

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Ætiology.—Newcomers to the endemic areas and Europeans are more liable than natives or long residents. Apparently, long residence confers a relative immunity, although not an absolute exemption.

All ages and both sexes are susceptible; but, in consequence of their habits and more frequent exposure to the predisposing and immediate causes, men are more subject to siriasis than are women.

Predisposing influences similar to those in heat-syncope and sun-traumatism powerfully influence the liability to siriasis. Amongst these are all physiological depressants; notably intemperance, fatigue, overcrowding, unsuitable clothing, malaria, acute disease, and, also, chronic organic diseases of the important viscera.

Siriasis has generally been attributed to a direct action of atmospheric or solar heat on the body. Many theories of the *modus operandi* of this assumed cause have been advanced. Among these may be mentioned superheating of the blood by the high temperature of the surrounding atmosphere; paralysis of the thermic centres causing (*a*) over-production of heat, or (*b*) retention of body-heat; pressure on the brain by expansion from heating of the cerebro-spinal fluid; vaso-motor paresis; paresis of the heart ganglia; excess of carbonic acid in the blood; coagulation of myosin; suppression of sweat; deficient serosity of the blood from excessive sweating, and so forth.

It is well known that neither high atmospheric temperature *per se*, nor high bodily temperature, unless the latter be associated with some special toxins, gives rise to symptoms at all like those of siriasis. Considering these two facts, and at the same time the peculiar and capricious distribution of the disease, the circumstances that its prevalence curve does not always correspond with the atmospheric temperature curve; that the degree of prevalence varies in the endemic area from year to year; that it is not most prevalent in the hottest years, seasons, or places; that it becomes epidemic at times; that it runs a definite course; that it may

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relapse; that in many instances it has definite premonitory symptoms; that it has peculiar lesions; and that it tends to terminate by crisis; in other words, that it behaves like pneumonia or any other specific fever, Sambon has boldly asserted that siriasis is a germ disease, like yellow fever or dengue, and, like these, is caused by some organism which demands for its development a high atmospheric temperature and certain, as yet unknown, local conditions. Time will show how far this hypothesis is correct. In my opinion it has more in its favour than any of the many theories that have been based on a purely thermic ætiology.

Symptoms.—Though sometimes coming on suddenly during exposure to the sun, siriasis is very often preceded by a distinct prodromal stage. It is very often developed independently of any direct exposure to the sun; not unfrequently the attack comes on during the night.

Among prodromata which may show themselves with greater or less distinctness for an hour or two, or even for a day or two, before the full development of the attack, may be mentioned great disinclination for exertion, pains in the limbs, drowsiness, vertigo, headache, mental confusion, sighing, anorexia, thirst, intolerance of light—sometimes accompanied by chromatic aberrations of vision—suffused eyes, nausea and perhaps vomiting, præcordial anxiety, sometimes a sense of impending calamity, a hysterical tendency to weep, a very hot dry skin, and a quickened pulse. Longmore called attention to excessive irritability of the bladder as a common prodromal symptom. This is a valuable and easily recognised danger-signal when present, and one the significance of which has been confirmed and emphasised by subsequent writers; it is possible, however, that its frequency has been exaggerated.

Though generally present in greater or less degree, and for a longer or shorter time, in many instances these prodromal symptoms are not remarked, the first indication of anything wrong being perhaps a short stage of restlessness, or possibly of wild

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delirium. This brief preliminary stage rapidly culminates in coma, complete unconsciousness, and high fever, quickly passing into hyperpyrexia.

Wood thus describes the symptoms of the developed attack:—"Total insensibility was always present, with, in rare instances, delirium of the talkative form, and still more rarely the capability of being roused by shaking or shouting. The breathing was always affected, sometimes rapid, sometimes deep and laboured, often stertorous, and not rarely accompanied by the rattle of mucus in the trachea. The face was often deeply suffused, sometimes with the whole face deeply cyanosed. The conjunctiva was often injected, the pupils various—sometimes dilated, sometimes nearly normal, sometimes contracted. The skin was always intensely hot, and generally, but not always, dry; when not dry it was bathed in a profuse perspiration. The intense burning heat of the skin, both as felt by the hand and measured by the thermometer, was one of the most marked features of the cases. The degree of heat reached during life was, in my cases, mostly 108°–109°. The pulse was always exceedingly rapid, and early in the disease often wanting in force and volume; later it became irregular, intermittent, and thready. The motor nervous system was profoundly affected. Subsultus tendinum was a very common symptom; great restlessness was also very often present, and sometimes partial spasms or even violent general convulsions. The latter were at times epileptiform, occurring spontaneously, or they were tetanoid, and excited by the slightest irritation. Sometimes the spinal cord appeared to be paralysed, the patient absolutely not moving."

The pupils, unless immediately before death, when along with the other sphincters they relax, are contracted. The reflexes are partially or wholly in abeyance. There may also be, especially in the graver cases, free watery purging, the dejecta, as well as the skin of the patient, emitting a peculiar and distinctive mousey odour. The scanty urine may contain blood corpuscles, albumin, and casts.

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Different writers mention a variety of what may be described as minor symptoms. They vary in different cases, and are by no means always present or characteristic. Whether these minor symptoms are present or not, in siriasis the essential symptoms—high fever and profound nervous disturbance, generally associated with insensibility—are invariably in evidence.

Unless active measures to lower temperature are taken early in the progress of the case, and unless these measures are vigorously carried out, in the great majority of instances death will occur within a few hours, or even minutes, of the onset of insensibility. The immediate cause of death is generally the failure of respiration. Rarely do cases linger for a day or two. Partial recovery is sometimes followed by relapse. In favourable cases the disease usually terminates by crisis. Convalescence is rapid.

Mortality.—As might be supposed, some types of heat-stroke are much more dangerous than others; siriasis infinitely more so than ordinary heat-exhaustion. Treatment, if early instituted and judiciously carried out, has undoubtedly a powerful influence in reducing mortality. Taking one type of heat-stroke with another, the case mortality among English troops in India is about one in four; in the year 1892, of 223 European soldiers admitted to hospital for heat-stroke 61 died.

Morbid anatomy.—A notable feature is the early appearance of *rigor mortis*. The blood is remarkably fluid, or but feebly clotted. The venous system is loaded, dark fluid blood pouring from the phenomenally engorged lungs and other viscera on section. Both blood and muscles are said to yield an acid reaction more or less pronounced. It has been stated that the red blood corpuscles are crenated, and do not form rouleaux. If the *post-mortem* examination is made shortly after death and before decomposition changes have set in, the heart in early *rigor mortis*, particularly the left ventricle, will be found to be remarkably rigid; this rigidity is sometimes described as being of woodeny hardness.

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There may be some venous congestion of the meninges, but the brain itself shows no important vascular, or naked-eye, changes. The intestinal mucosa, as well as that of the stomach, is swollen and exhibits patches of congestion.

Pathology.—As may be gathered from the remarks on ætiology, the pathology of siriasis, so far, is in a very unsettled state, and will continue to be so until the essential cause of the disease has been finally determined.

Diagnosis.—The presence of high fever is sufficient to differentiate siriasis from sudden insensibility caused by uræmia, by diabetic coma, by alcoholic and opium poisoning, and by all similar toxic conditions. Cerebral hæmorrhage, particularly pontine, may, after some hours, be followed by high temperature; but here the febrile condition follows the insensibility, whereas in heat-stroke the febrile condition precedes insensibility. The diagnosis from a cerebral malarial attack may be very difficult; chief reliance has to be placed on the history—if obtainable, on the condition of the spleen, and, especially, on the result of microscopic examination of the blood. Malarial fevers, and the early stages of the eruptive fevers in children, are very apt to be regarded as heat-stroke, particularly if there has been recent exposure to a hot sun. Cerebro-spinal fever, so often mistaken for siriasis, may be recognised by the occipital retraction, the irregular pupils, the frequent occurrence of strabismus, the comparatively low and fluctuating temperature, the associated herpes, the initial rigor, and its long duration.

Treatment.—In all fulminating fevers, including siriasis, occurring in warm climates, if malaria be suspected, particularly if the parasite be discovered in the blood, quinine should be injected hypodermically at once—seven to ten grains of the bihydrochloride; this dose should be repeated three or four times at intervals of four hours. In every case of siriasis, whether it has been deemed advisable to administer quinine or not, attention must at once be given to reduce temperature by such rapidly-acting measures as the

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cold bath, or ice applied in various ways to the head and body. Antipyretic drugs are of very little service, even if, in consequence of their depressing action on the heart, they be not actually dangerous; in all serious cases of siriasis, such drugs must be carefully avoided. Chandler, speaking from an experience of 197 cases in which the mortality amounted only to twelve, gives some excellent directions for the management of hyperpyrexial cases. He directs that the patient be placed undressed on a stretcher, the head end of which is raised slightly so as to facilitate the escape of involuntary evacuations and to provide for drainage. A thermometer is kept in the rectum. The body is covered with a sheet upon which are laid numerous small pieces of ice, larger pieces being closely packed about the head. Iced water is then allowed to drip for thirty or forty minutes on the patient from drippers hung at an elevation of from five to ten feet. A fine stream of iced water poured on the forehead from an elevation will act as a stimulant and rouser; this is a very powerful measure, and must not be kept up for longer than one or two minutes. A hypodermic injection of forty minims of tincture of digitalis is given as soon as possible, its administration being preceded in the case of plethoric patients showing much arterial tension (but not otherwise) by a small bleeding. The application of cold should be at once discontinued so soon as the thermometer in the rectum has sunk to 104°, or, in cases of simple thermic fever in which the temperature has not exceeded 106°, when it has fallen to 102°. If these powerful antipyretic measures are carried beyond this point the fall of temperature may continue below the normal, even to as low as 91°, and dangerous collapse ensue.

On discontinuing the iced sheet, the patient should be wrapped in a blanket, and hot bottles applied to limbs and trunk. Very likely perspiration, a very favourable sign, will then set in. Stimulants may now be necessary. Strychnine, owing to the marked tendency to convulsions present in heat-stroke, must on no account be used

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as a cardiac stimulant. Convulsions are best controlled by cautious chloroform inhalations. As death in heat-stroke generally results from failure of respiration, Chandler strongly recommends artificial respiration when the breathing threatens to become suspended ; he claims to have obtained some marvellous results from this expedient. It should be kept up for half an hour or longer.

During convalescence great care must be exercised to shield the patient from all influences calculated to provoke relapse.

SUN-TRAUMATISM.

There is a large, ill-defined, and difficult-to-define class of heat-stroke cases, which belong neither to the category of heat-exhaustion nor to the very definite and probably specific disease just described. The morbid phenomena in this class of sun-induced disease are attributable, apparently, to a peculiar physical action of the direct rays of the sun on the tissues. To this category belong, it seems to me, those sudden deaths occurring without warning during, and manifestly in consequence of exposure to the sun. Such may have been the sudden deaths described by Parkes, Maclean, Fayrer and others, in which soldiers in the excitement and stress of battle, while oppressed with thick clothing and heavy accoutrements and exposed to a blazing sun, suddenly fell forward on their faces and, after a few convulsive gasps, died. In these instantaneously fatal cases the paralysis of the heart or respiration seems to be of the nature of shock, as from a blow or other sudden and violent impression on the encephalon.

Doubtless, indeed it is a well-known fact, the strain undergone in these and similar circumstances may, in some instances, cause an apoplexy or rupture of some description in tissues prepared for such a cataclysm by morbid degenerations of long standing.

Besides the foregoing there is another type of case in which, after prolonged exposure to the sun, a febrile condition is established. This is sometimes of great severity, being characterised by intense headache, a

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rapid full pulse, a pungent dry skin, intolerance of light, sound and movement, and occasionally by vomiting or delirium. This condition suggests meningeal congestion, possibly inflammation. The acute phase may be quickly recovered from, or it may prove very persistent and last for days or weeks. It may leave no injurious effects; or it may be followed by a variety of transient or more permanent morbid nervous phenomena. Among the sequelæ authors have mentioned tremor, loss of memory, amaurosis, deafness, various paretic conditions, epilepsy, insanity, persistent headache, recurring headache, dyspeptic conditions. How far these sequelæ are entirely attributable to sun-exposure, or how far they depend on independent diseases, as syphilis for example, the local cerebral manifestations of which may have been provoked, though not actually caused, by the sun-traumatism, it is not always easy to say.

The **morbid anatomy,** as well as the clinical symptoms, indicates meningitis as a feature in these instances of reputed sun-traumatism. Authors refer to thickenings and opacities of the meninges, and even to thickening and roughening of the calvarium.

Many speculations have been advanced as to the **pathogenesis.** Manifestly it is not altogether, if at all, a question of caloric, for such effects do not result from exposure to the heat of a furnace, however intense. There appears to be some special element in the solar spectrum capable of injuriously affecting the tissues, particularly if they have not become gradually habituated to sun-exposure. That some such element does exist is proved by the phenomena of sun-erythema, of that form of skin pigmentation known as sun-burning, and, possibly, of leucodermia. The sensation of distress brought on by exposure to a hot sun, which is quite a different sensation from that produced by the heat of a fire, points in the same direction. In this connection we are forcibly reminded of the phenomena of the actinic rays of the solar spectrum, and of the remarkable tissue changes induced by the Röntgen rays.

Treatment.—Patients suffering from sun-trau-

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matism must be kept as quiet as possible in a cool, airy, and darkened room. For a time the head should be kept shaved, and cold applied to the scalp. The bowels must be free; food should be light and unstimulating, and alcohol in every form strictly forbidden. Restlessness and insomnia are best treated by the bromides. For a considerable time the patient will be conscious of loss of memory, and feebleness of intellectual power and of the faculty of concentration. He may be irritable, liable to headache, and extremely sensitive to heat—more particularly the heat and glare of the sun. So soon as he is able to be moved he must be sent to a cold climate, and there remain until all trace of his illness has completely disappeared. Indeed, it is questionable if the subject of pronounced sun-trauma should ever again risk the dangers of a tropical climate; certain it is that he should not return to the tropics so long as the slightest evidence of cerebral trouble remains.

For persistent headache and other signs of chronic meningitis, courses of the iodides and bromides, repeated blistering of the neck and scalp, together with careful dieting and general hygiene, should be tried. In not a few instances, in spite of the most careful treatment, medicinal and climatic, serious permanent disease of the encephalon remains, giving rise to various and often incurable troubles, and, very commonly, to distressing intellectual enfeeblement.

PREVENTION OF HEAT-STROKE.

In heat-stroke climates great attention should be paid to the general health; if this be not satisfactory, exposure to the sun and to high temperatures must, so far as possible, be avoided. Alcoholic drinks, gluttony, excess of animal food, too much tobacco smoking, in fact dissipation of all sorts, are especially to be deprecated. Individuals suffering from malarial or other fevers, or from chronic liver or kidney disease, run great risk if they are careless about exposing themselves to the sun. Violent exercise, excessive fatigue, want of sleep, constipation, are also to be avoided.

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Clothing ought to be light and loose fitting, the under-garment being of thin woollen material. In going out in the sun the head must be protected by a wide-brimmed, well-ventilated pith hat shielding the temples and neck as well as the top of the head. An actinic theory of sun-traumatism, advocated many years ago by Maude and Duncan, and more recently by Sambon (*Jour. of Trop. Med.*, Feb. 15, Mar. 1, 1907), indicates the necessity for a radical change in the colour of the dress materials now in vogue among Europeans in the tropics. The natives of warm climates invariably have dark skins; a natural provision of protection against the actinic rays of the solar spectrum. Exposure to the sun tans the European; a natural protective reaction. Therefore the European in the tropics, conformably to this hint from nature, should invariably wear non-actinic colours—a red or yellow shirt, or a fabric (solaro) such as is now manufactured into which these colours enter. The sun-hat should be similarly guarded. Experience has shown the comfort and value of such an arrangement. A pad of cotton sewn into the back of the coat in such a way as to protect the spine is a wise measure, and one adopted by experienced sportsmen in India. The phenomena connected with the Röntgen rays suggest the possibility that there may be solar rays other than the ordinary heat and actinic rays, which, although they may be able to pass through organic materials, can nevertheless be arrested by metals. If this be true for the sun as well as for the Röntgen rays, a useful addition to the sun hat would be a thin plate of some light metal placed between the layers of pith constituting the basis of the ordinary solar topee. A sheet of tinfoil or other light metal would not perceptibly add to the weight of the head-gear. Such sun-hats are, I believe, now manufactured. A white umbrella, lined with green or orange, ought never to be despised. Tinted (smoke colour) goggles are probably a protection, as they certainly are a great comfort in mitigating solar glare.

Rooms should be kept dark during the day, and cooled by means of punkahs, thermantidotes, tatties,

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venetians, and other contrivances. In barracks and ships there must be no overcrowding. In very hot weather European soldiers should, if possible, sleep under punkahs. Military drills should be reduced to a minimum, and take place in the cool of the morning only, and after the soldier has had a cup of tea or coffee and some light food. Marches should be short, interrupted by frequent halts, and be got through if possible in the early morning. While marching the men ought to be in open order, relieved of all unnecessary weights, belts and clothing, and well supplied with water. Camps should be pitched in cool and airy spots and on turf and under large spreading trees free from undergrowth. Double canvas, one layer of which should be non-actinic, and grass or boughs laid on the wall of the tent, will do much to mitigate the temperature within.

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SECTION II.—GENERAL DISEASES OF UNDETERMINED NATURE

CHAPTER XXIV

BERIBERI (KAKKE, BARBIERS)

Definition.—Beriberi is a specific form of multiple peripheral neuritis occurring endemically, or as an epidemic, in most tropical and sub-tropical climates, and, also, under certain artificial conditions, in more temperate latitudes. The mortality is considerable, death usually depending on heart paresis.

Historical.—The special nature of beriberi was recognised by the Dutch in the early years of their intercourse with the East. Later, it was studied by British physicians in India, particularly by Malcomsen, Carter, Waring, and Morehead. It was not until a more recent epidemic in Brazil that beriberi began to receive attention from the present generation of medical men; and it was not until Anderson, Simmons, Scheube, and Baelz took up the subject in Japan that it was studied by modern methods, accurately defined, and its true pathology apprehended. Scheube and Baelz were the first to show distinctly that beriberi is of the nature of a specific peripheral neuritis similar to that of diphtheria and alcohol, a view which was subsequently confirmed and adopted by Pekelharing and Winkler, and by most subsequent observers.

Geographical distribution.—The area of the endemic distribution of beriberi is co extensive probably with the tropical and sub-tropical belts; doubtless it exists in many places where its presence is not generally suspected. It is the scourge of many of the mines and plantations of the Malay and Eastern Archipelago. It is apt to break out among the coolie gangs engaged on extensive engineering

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works in the tropics, such as the Panama Canal or the Congo railway. It haunts the Dutch army in Sumatra, and used to be common enough, until better hygienic methods prevailed, in the British armies in India. It is at home in many parts of Japan, particularly in her large, low-lying, damp, over-crowded cities. It occurs in China, Manila, the Eastern Peninsula, India, and Africa. It is prone to break out in gaols, in schools, in ships. Sometimes, as an epidemic wave, it passes over a tropical country, as was the case in the early 'sixties in Brazil, where it still lingers. Sometimes sporadic cases crop up here and there. Generally, when it appears in a community, it attacks large numbers, picking out particular houses and districts. Lately we had an account of a small epidemic among a group of Western Australian natives, and also among Chinese on the eastern seaboard of Australia, a continent where beriberi was formerly supposed not to exist. Similarly, it appeared lately, apparently for the first time, in Japanese immigrants in Fiji. A little while ago I saw a case having the history and clinical features of beriberi from Lake Nyassa, another from the Upper Congo, another from Hayti. We hear of it also from Havana, from New Caledonia, from the Sandwich Islands, from Uganda—all of them places not before known to be liable to this disease. So that the area of distribution is an extensive one. Indeed, within the last few years it would seem that it includes the temperate as well as the tropical zones. Recently beriberi showed itself in a lunatic asylum in Ireland—Richmond Asylum, Dublin; and apparently the same disease has been seen lately in lunatic asylums in the United States and in France, and also among the fishermen on the North American coast.

Symptoms.—Medical visitors to the native hospitals in many parts of the tropical world are likely to have their attention arrested by the large proportion of cases of partial paraplegia, of cases of œdema of the legs, and of cases of general dropsy. These, for the most part, are cases of beriberi.

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Paraplegic cases.—On examining one of the paraplegic cases referred to (Fig. 57), it will be found that, besides paraplegia of greater or lesser degree, there is a certain amount of anæsthesia or of numbness of the skin; particularly of the skin over the front of the tibiæ, the dorsa of the feet, the sides of the thighs, perhaps also of the finger tips, and of one or two areas on the arms and trunk. The visitor may be struck with the thinness of the patient's calves, the flabby state of the gastrocnemii; and by the fact that if, whilst making the examination, he should handle these and the neighbouring muscles somewhat roughly, particularly if he should squeeze them against the underlying bones, the patient will call out in pain and try to drag the limb away. The thigh muscles may be found to be similarly tender, and so may the thenar, the hypothenar, and the arm muscles; like the calf muscles, these too may be wasted and flabby. Very probably there is a loss of fat as well, the panniculus adiposus being everywhere very meagre. If tested electrically, the muscles exhibit to perfection the reaction of degeneration. If the knee reflex be tested in the usual way, after the first week of the disease there will be no response

Fig. 57.—Paraplegic beriberi. (*Bentley.*)

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whatever; nor can any clonus be elicited. As a rule, all the deep reflexes are lost; but the superficial reflexes, unless in extreme conditions of paresis and muscular atrophy, are usually present and more or less active. If, in severe cases, the patient is set to button his jacket or to pick up a pin, possibly he has a difficulty about it, or perhaps he cannot; he may bungle and fumble like an advanced ataxic.

There is more than ataxia, however; for the hand grasp is so enfeebled that the patient may have a difficulty in holding his rice bowl as well as in feeding himself. There is no tremor of the hands; and never or very rarely is there any paresis of the ocular muscles, or of the muscles of the face, of mastication, of the tongue, or of the pharynx. The sphincters and bladder operate satisfactorily, and the functions of the alimentary canal are carried on fairly well, although there is often some dyspeptic distension and oppression after food. On the patient being got out of bed and started to walk, if he is able to progress at all, his gait will be markedly ataxic; but he is not ataxic merely, for, just as with the hands, it will be seen that, in addition to want of co-ordinating power, there is great muscular weakness. If he is laid on the bed and asked to raise his legs, he is perhaps hardly able to get them off the mat, to cross them, or to place them one foot on top of the other. Very probably he is the subject of marked ankle-drop, so that he drags his toes when he attempts in walking to advance the foot; he has therefore to raise the foot very high, letting it fall on the ground with a flop when he brings it down again. His ataxia and his muscular weakness, as well as the partial anæsthesia from which he suffers, force him to adopt a variety of devices to assist him in progression (Fig. 58). Manifestly these patients are suffering from some form of peripheral neuritis.

The general health is good for the most part; the tongue is clean, the bowels are fairly regular, and there is nothing amiss with the urine. Digestion, assimilation, and excretion go on satisfactorily.

The heart and circulation. — When the heart is

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examined, if the case be at all recent or moderately severe, attention is at once arrested. On inspection it may be remarked that the impulse is diffuse, that there is epigastric pulsation; that the carotids throb

Fig. 58.—Paraplegic beriberi. (*Bentley.*)

too violently; that there is that peculiar wobbling, pulsating movement in the jugulars that denotes tricuspid insufficiency. On percussion the præcordial area is frequently found to be enlarged, perhaps very greatly enlarged, especially to the right; and on aus-

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cultation loud bruits, usually systolic in rhythm, may be heard. Marked reduplication of the sounds, particularly of the second sound, is to be noted. The auscultator may in a large proportion of cases also be struck by the peculiar spacing of the intervals between the sounds. It may be hardly possible to tell by the ear alone which is the first pause and which is the second. They seem alike in point of duration; so that the sounds of the heart are, like the beats of a well-hung pendulum clock, evenly spaced, and not, as they are in health, separated by a long and a short interval, like the beats of an ill-hung clock. It will also be observed that the heart is very irritable, becoming easily quickened by exertion. It will be judged, therefore, that, in addition to peripheral neuritis, there is serious disease in the circulatory system, particularly in its innervation; that there is dilatation of the right side of the heart; and that there is a state of relaxed arterial tension.

All these signs and symptoms vary in degree from time to time in the same case, and differ in degree in different cases.

Dropsical cases.—In the next bed, perhaps, to the patient whose picture I have tried to draw, may be seen another man suffering from apparently quite a different affection (Fig. 59). He is propped up in bed. Instead of being thin and wasted, as the last patient, his face is puffy and heavy; his lips possibly are slightly cyanosed; and his arms, hands, trunk, legs, and feet are distended with œdema. It may be thought from the œdema that it is a case of acute nephritis; but an examination of the scanty, dark-coloured urine shows that it is of high specific gravity, and contains no albumin, or only a mere trace; so that the case cannot be one of acute Bright's disease. Careful observation will discover that the œdema is somewhat firmer than that of nephritis, and, in not a few instances, that it does not involve the scrotum. Occasionally cases are met with in which the œdema is peculiarly localised and fugitive. If attention is directed to the heart, a bruit and other evidences of dilatation of the organ and of arterial relaxation,

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just as in the first case, are discovered. If the lungs are examined, one may or may not discover signs of single or double hydrothorax, although, probably, not to a very great extent. The lungs themselves are healthy. On getting him out of bed it is found that the patient can hardly walk; partly from breathlessness, partly on account of mechanical interference by the dropsy with the movements of the legs, partly, perhaps, from some degree of paresis. He has ankle-drop possibly; and, if firm pressure be brought to bear on the calf muscles through the œdema, signs of hyperæsthesia of the muscles may or may not be elicited. Knee-jerk is probably absent, and there is numbness of the shins and finger-tips. The tongue is clean, the appetite fair, and there is no fever. But there may be complaint of præcordial distress and even pain and, as this is aggravated by a full meal, the patient eats sparingly. The amount of urine is generally very much reduced—to a few ounces even.

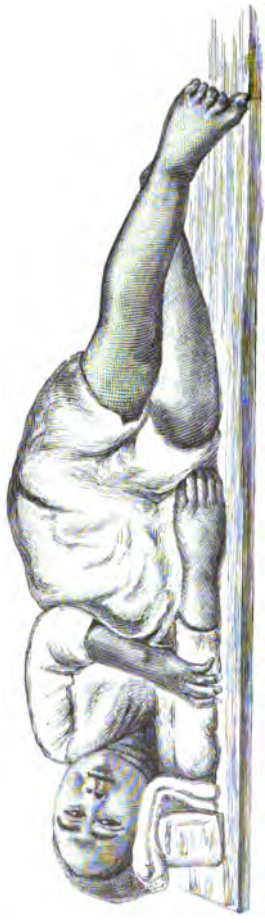

Fig. 59.—Dropsical beriberi. (*Bentley.*)

In this patient, therefore, there are the same signs of peripheral neuritis and of dilatation of the heart

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as in the other case. In addition, there is a somewhat firm œdema, which is not altogether cardiac, but, as its character and the circumstances in which it is found suggest, is probably connected partly with lesion of the nerves regulating urinary excretion, and partly with the play of transudation and absorption in the connective tissues.

Mixed paraplegic and dropsical cases. — In the next bed to this patient there lies, perhaps, another case which looks like a mixture of the two preceding. There is œdema—generally somewhat firm—particularly of the shins and feet, about the flanks, sacral region and, very generally, over the sternum and root of the neck. There is numbness of the shins, there is some ataxia, there is muscular weakness and hyperæsthesia—particularly of leg and thigh muscles, there is absence of knee-jerks, there is probably a cardiac bruit and reduplication of sounds, and there are signs of dilatation of the heart and relaxed arterial tension. Just as in the other cases, the general health of the patient is unaffected, the tongue is clean, the urine though scanty is otherwise normal, and there is no fever.

Great variety in degree and combination of symptoms. — All through the wards of the hospital similar cases may be encountered. Some are so trifling that they are up and moving about with more or less freedom; others are so severely smitten that they lie like logs in their beds, unable to move a limb or perhaps even a finger. Some are atrophied to skeletons; others are swollen out with dropsy; and some show just sufficient dropsy to conceal the atrophy the muscles have undergone. Although the cranial nerves above the seventh are very rarely involved, in some it will be noticed that the laryngeal muscles are paralysed, the patient being unable to speak above a whisper or to produce an explosive cough. In one or two cases the abdominal and the perineal muscles may be so profoundly paralysed that, when cough is attempted, at most a husky expiration is produced, whilst the belly is bulged forwards and the perineum shot downwards

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by the sudden contraction of the muscles of expiration. In practically all cases of over a fortnight's standing the knee-jerk and tendo achillis reflex are absent; at the very commencement of the disease these deep reflexes are exaggerated, gradually disappearing as symptoms develop, not to reappear for months, perhaps, after the patient is well in all other respects.

Erroneous diagnoses.—The novice in tropical medicine will be greatly puzzled for a time over these cases. I have seen them called cardiac disease, locomotor ataxia, muscular rheumatism, progressive muscular atrophy, ascending spinal paralysis, and have over and over again seen them relegated to that refuge for ignorance—malaria, and called "malarial rheumatism," or "malarial paralysis," or, more pedantically, "malarial paraplegia," or "malarial neuritis." *

If the visitor has the curiosity to examine the blood of these patients, possibly in a proportion of them he will find *Filaria nocturna*, or some of the other bloodworms; very likely he will then think that the cases are forms of filariasis, and he may construct theories to explain how the filaria produces the symptoms. Or, if he examine the fæces, very probably in over 50 per cent. of the cases, or, in some countries, in nearly all the cases he will find the ova of *Ankylostomum duodenale* and, probably, those of *Tricocephalus dispar* also. On this evidence he may conclude that these are cases of ankylostomiasis. He had better, however, not commit himself to such a diagnosis until he has ascertained how it fares with the rest of the population as regards these parasites; for he will find that the filaria, the ankylostomum, and the trichocephalus are quite as prevalent

* Dr. Strachan has described (*Practitioner*, 1897, p. 477) a form of multiple peripheral neuritis which he calls "malarial." The disease is endemic, and very common in Jamaica. It differs from beriberi inasmuch as it is not attended with œdema, is frequently attended with implication of the cranial nerves, and is rarely fatal. We have no accounts of any similar disease from other tropical countries. Probably, therefore, Dr. Strachan's neuritis is not malarial, but depends on some cause peculiar, so far as known, to Jamaica. The subject requires further study.

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outside as inside the hospital, and in the healthy as in the sick.

Past history of patients.—On inquiry he will learn that most of the cases come from two or three centres where similar disease is endemic—from some particular plantation, mine, or village. He will also remark that the same places supply both atrophic-paralytic cases and dropsical-paralytic cases; and he will also learn that many of the atrophic cases commenced with dropsical symptoms. From this he will make the important deduction that he is dealing, not with two diseases, but with two phases of the same disease, which sometimes assumes atrophic features, sometimes dropsical features, and sometimes is of a mixed character. Some of the patients will give a history of fever at the outset of their troubles; in some there is a history of indigestion or diarrhœa; in some the paralytic or dropsical symptoms developed very slowly; in others, again, they came on rapidly. In some there is a history of a similar attack the previous year, or a yearly attack for three or four years in succession. Some will tell that they have been ill for several months, others that they have been ill for a week or two only.

Uncertain course.—The visitor will learn that this disease, which is beriberi, slowly or rapidly declares itself after an incubation period as yet undetermined but variously stated as of weeks or months, that it may be preceded by a period of intermitting languor, aching legs, palpitations, breathlessness, slowly advancing œdema of legs or face; or that the patient may wake up some morning and find that during the night he has become dropsical or paretic. Thus the disease may develop slowly or rapidly. Equally uncertain are its progress and danger; within a day or a week, or at any time during its course, it may assume fulminating, malignant characters. It may completely subside in a few days, or it may drag on for months. It may get well apparently and then relapse. It may, and generally does, clear up completely; or it may leave a dilated heart, or atrophied limb muscles with corresponding deformity. The

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variety in the severity, progress, and duration of beriberi is infinite; but in all cases the essential symptoms are the same—greater or less œdema, especially over the shins; muscular feebleness and hyperæsthesia, especially of the legs; numbness, especially over the front of the shins, of the finger-tips, occasionally of the lips; liability to palpitation from cardiac dilatation, and to sudden death from the same cause.

Progress of the cases.—As the visitor watches the progress of the cases he will be astonished that those which he thought examples of locomotor ataxia, or of progressive muscular atrophy, or of ascending spinal paralysis, gradually improve, begin to walk about, and finally quit the hospital quite well. He will be astonished to see, after perhaps a profuse diuresis, the bloated carcass, that could hardly turn itself in bed, rapidly shrivel to little more than skin and bone, and assume all the appearances of the atrophic cases; and, later, perhaps after many months, become rehabilitated, and, in due course, walk out of the hospital quite well. He will notice that the cardiac bruits come and go; that the degree of dilatation of the heart is subject to fluctuations; that what seemed organic disease completely disappears.

Cardiac attacks.—But he will also be astonished, as he goes his rounds, to see so often empty beds where the day before lay men whom he considered by no means seriously ill — certainly not dying. Some day he will come on a patient, whom the previous day he thought to be by no means seriously ill, actually *in extremis*. The poor fellow is propped up in bed, he is struggling for breath, his face is purple, his eyes are starting out of his head, his whole attitude is expressive of the utmost distress; he has a horrible, tearing, boring, crushing pain under his sternum and in the epigastrium; the vessels of his neck are throbbing violently, but his pulse is quick, small, intermittent, and his extremities are cold. In a short time the patient is dead. Some of the fatal cases, he will note, die quite suddenly as if from syncope; but most die in the distressing way described, evidently from paresis and over-distension of the right heart,

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complicated and aggravated by œdema of the lungs, or by diaphragmatic paralysis, by hydrothorax, or by hydropericardium.

Nomenclature and classification of beriberi.—For purposes of description, the paralytic-atrophic cases are designated "dry beriberi" or beriberia atrophica; the dropsical cases, "wet beriberi" or beriberia hydrops; and those in which there is a combination of both conditions, "mixed beriberi." Sometimes the cases are classified according to the rapidity of development and gravity of symptoms into acute or pernicious, subacute, and chronic. None of these classifications is good, seeing that they all refer to the same disease, and that one form may suddenly or more slowly merge into the other.

Hamilton Wright, whose views on the ætiology of the disease will be presently stated, classifies the cases as follows:—

Acute	Cardiac, Motor, Sensoro-motor or Vaso-motor	Beriberi.
Beriberi residual	Cardiac, Motor, Sensoro-motor or Vaso-motor	Paralysis.

Ætiology.—*Sex, age, occupation, etc.*—Beriberi attacks both sexes. Although rare in childhood and extreme old age, it occurs at all ages, its favourite age being from about fifteen to thirty. It affects rich as well as poor. It is confined to no particular trade or occupation. If anything, it has a predilection for those who lead a sedentary life and are much indoors, as students, prisoners, and the inmates of asylums. It is apt to attack pregnant or parturient females. It is quite as common in the strong and full-blooded as in the weak and anæmic.

Climatic conditions.—In countries in which there is a hot and cold season the epidemic outbreaks occur during the former, old cases improving and new cases ceasing to crop up during the winter. In countries which are hot all the year round beriberi may appear

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at any time; most frequently, however, in such climates it appears during the rains. Thus it resembles malaria in being fostered by damp, by high temperature, and by its most often attacking those who sleep on or near the ground. As with malaria, though its explosion in any given individual residing in the endemic area may be solicited by fatigue, chill, privation, and other causes of physiological depression, it is not actually caused by such circumstances. Unlike malaria, it is common enough in the midst of large cities, as well as in villages and jungle lands.

Influence of overcrowding.—Overcrowding seems to favour the outbreak, or rather, the spread of beriberi. This has, perhaps, a good deal to do with its frequency and virulence in Oriental gaols, schools, mining camps, plantation lines, armies, ships.

Ship beriberi.—Unlike malaria, beriberi is common in the native crews, more rarely, though occasionally, among the European officers and sailors, of ships on the high seas and far away from any recent telluric influence. The crowding in the damp forecastle and the exposure incident to a sailor's life seem to be among the reasons, though not the only ones, for ship beriberi. Thus, this form of the disease is often seen at the Seamen's Hospitals at the Albert Docks and Greenwich among the lascars and sidi-boys of steamers trading to India, the disease appearing perhaps months after the ships have left the East, sometimes even months after they have been lying in the London Docks. Some years ago a number of these cases were admitted to the Seamen's Hospital at the Albert Docks. I had the curiosity to visit one of the ships from which several of the patients had been brought. I went into the forecastle. Although the weather was mild for Englishmen, it was evidently very cold for the half-clothed lascars. They had a fire blazing in their quarters, every door, scuttle, window, and ventilator of which they had carefully closed. The place was suffocatingly hot, damp, and redolent of steaming humanity. I do not know how many men had stowed themselves away with their dirty rags in this place, but there was a crowd of them. Several had

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symptoms of beriberi, and were in their bunks. After seeing the forecastle I was taken to a little dark cell, an oblong den with a couple of bunks one on top of the other, located somewhere in the neighbourhood of the keel. There was no light or obvious means of ventilation, and barely standing room. There I found three men sitting on the lowermost bunk, all of them suffering from severe beriberi. One of them, I afterwards heard, died before morning; the others were sent to the hospital just in time, I believe, to save their lives. The fact is that some of these epidemics of ship beriberi in cold climates are fostered by the artificial conditions which the ignorant lascars are allowed to bring about. They feel the cold of the English climate so much that, on entering British seas, they try to keep their quarters warm by lighting fires and stopping up ventilators. By these means they create a hot, steamy atmosphere and a sodden state of the place they live and sleep in, which is a very good imitation of the tropical conditions the germ of beriberi requires for its development. In other words, these lascar sailors create an incubator on a large scale, which, should it chance to contain a beriberi germ, quickly becomes extensively infected and lethal. For some unknown reason beriberi is very common in Swedish and Norwegian ships.

Asylum beriberi.—Not very long ago exactly similar conditions to those above described, and with similar results, were produced by similar means in the Dublin lunatic asylum already alluded to. This asylum, built for 1,000 inmates, had 1,500 crowded into it. Anyone who knows what the atmosphere of even a well-regulated and not overcrowded dormitory in a lunatic asylum is like, can imagine what it becomes in warm weather, when three patients are lodged in a place barely sufficient for two. The heat, the breath-vapour condensed and streaming down the walls, the effluvia from the patients, the closed doors, the barred windows, the want of air, and the damp conspire to foster any germ of beriberi which evil chance may introduce into this incubator. These are just the conditions found in the tropics; and it may be

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that when such conditions are reproduced elsewhere, even in temperate climates, on the beriberi germ being accidentally supplied from without, the result will be just the same.

Beriberi a germ disease, but not easily communicated from man to man.—Beriberi is undoubtedly a germ disease, for, as not a few facts have shown, the cause can be transported from place to place and, on encountering suitable conditions, multiply as only a living organism can. This is about the limit of our actual knowledge. What the germ may be or even what may be the medium it multiplies in—whether the human body, food, soil, or other surroundings—is not definitely known. I do not think that the germ passes directly from one human being to another like the germ of the ordinary infectious or directly communicable diseases. Nurses and medical men in hospitals where, perhaps, there may be hundreds of beriberi patients, do not catch the disease; nor in hospitals located outside the endemic districts does it spread to other patients. Of course, if hospitals are themselves infective, are themselves beriberi centres, beriberi may in that case attack patients admitted for other diseases, particularly, I think I have observed, for surgical disease and operation cases; in these circumstances it may attack nurses and medical attendants. Beriberi resembles malaria and yellow fever in some of these respects.

Theories as to the cause of beriberi.—Beriberi has been attributed to a great variety of causes. Many of these are so manifestly erroneous that they need not be discussed, as, for example, malaria, intestinal worms, scorbutus. Others, although with more in their support, having been disproved may also be dismissed. Such are the bacteria of Pekelharing and Winkler and many other observers who, in consequence of imperfect technique, came to regard ordinary skin bacteria as blood-borne pathogenic organisms. Such too is the suggestion made by Ross, on the ground that arsenic is present in the hair of some beriberics, that the neuritis of beriberi was an arsenical neuritis, a suggestion that many careful

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analyses and observations, made with this point in view, have not substantiated. Such too is the theory that attributed beriberi to nitrogen starvation—to deficiency of nitrogenous elements in the dietary. In former years, beriberi used annually to attack quite one-fourth of the *personnel* of the Japanese navy. Now it is almost unknown in that service. The striking change coincided, in point of time, with the introduction into the Imperial navy of an improved ration, in accordance with a suggestion from Takaki, who entertained this view about the influence of deficient nitrogen in food. It was inferred from the success following the change that the improvement in the health of the sailors was attributable to the increased amount of nitrogen in the new dietary. But the improvement could have been no more than coincidence; or, at most, the influence of the increased supply of nitrogen could only have been subsidiary. For although an improvement in the diet coincided with a decrease in the amount of beriberi in the fleets, barracks, and prisons of Japan, a similar modification of diet had no similarly satisfactory sequel in the prisons of the Straits Settlements or elsewhere. In the case of Japan there were other hygienic reforms introduced about the same time as the improved dietary; these, doubtless, had their favourable influence.

Lately a French writer, on the strength of a limited number of observations on the curative and preventive influence of a fat dietary in beriberi, has propounded the theory that the disease is caused by deficiency of this element in the food.

If we examine all the circumstances, we shall find that neither the nitrogen starvation theory nor the fat starvation theory tallies with the facts of the peculiar geographical distribution of beriberi, its peculiar local limitations, its affecting rich as well as poor, its appearing in some houses and not appearing in neighbouring houses, and many other facts. Up to the present we have no information that would justify a pronouncement as to whether the beriberi germ is a fungus, a bacterium, or a protozoon. Such data as we do possess justify speculation only as to

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the medium in which the germ operates, and as to how the morbid influence is conveyed from place to place and to man.

The germ viewed as producing a toxin in food.—It has been definitely proved that beriberi is not conveyed by water; on the other hand it has often been asserted that it is conveyed in food, especially damaged food—damaged fish, and damaged rice. Durham has definitely excluded damaged fish, and it may also be safely concluded that damaged rice—mouldy rice—is equally innocent. Braddon, however, has advanced the view that under certain circumstances rice is really the medium through which the germ operates.

This observer, fixing his attention on the remarkable and admitted fact that of the various races inhabiting the Malay peninsula the Chinese are infinitely the most subject, the Klings (an immigrant Indian race) infinitely the least subject to beriberi, comes to the conclusion that the excessive liability of the one race and immunity of the other are attributable to the difference in the way in which their staple food—rice—is prepared for the market. The Klings live on what Braddon calls "cured rice," that is rice which when garnered, and before husking, is boiled and dried. The Chinese use "uncured rice," that is rice that is husked without preliminary boiling. Braddon holds that rice (*padi*) is liable in certain localities to be attacked by a germ which in its multiplication produces a toxin, and that this toxin, which is not destroyed by cooking, is the cause of beriberi. The germ is destroyed by the boiling to which "cured rice" is subjected before husking; hence the freedom of the Klings from beriberi and the excessive liability of the Chinese. That there is no racial insusceptibility in the Klings is proved by their being attacked by beriberi when they chance to get imprisoned and are placed on the same food as their Chinese fellow-prisoners.

Although there is much to be said in favour of this and some other food theories of beriberi, they have all been greatly impugned by certain experi-

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ments carried out by Travers, at Kwala Lumpur. There are two gaols in that city. One was the seat of an extensive and persistent epidemic of beriberi, whilst the other remained healthy. Travers caused the rice supplied to the prisoners in the healthy gaol to be taken from the same stock of grain, and to be cooked in the same vessels, as that supplied to the prisoners in the beriberi-stricken gaol. The prisoners in the healthy gaol remained healthy, and beriberics sent there from the unhealthy gaol usually rapidly recovered. This experiment was prolonged and apparently scrupulously conducted.

On the other hand Braddon's views have received support from a carefully conducted experiment by Fraser and Stanton, who fed a gang of coolies on cured rice and another gang on uncured rice, both sets of coolies being in other respects under apparently identical conditions, with the result that many of those on uncured rice sickened with beriberi, whilst many of those on cured rice escaped the disease. Moreover, it has been stated that since the inmates of the public institution in the Straits Settlements and F.M.S. have been placed on cured rice beriberi, formerly exceedingly prevalent, has disappeared.

The germ viewed as a saprophyte and producing a toxin in external surroundings.—According to this view the toxin of beriberi produces neuritis much in the same way that alcohol does. The soil or surroundings are the infected medium; the man residing on or in these is poisoned, not infected. In the case of alcoholic neuritis—so like beriberi—the germ of the disease is the yeast plant; the culture medium, the saccharine solution; the toxin, the alcohol. The alcohol germ may be swallowed with impunity; not so the toxin it generates. So with beriberi: its germ lives in the soil, house or ship; under certain conditions of temperature and moisture it proliferates and produces some kind of toxin there; and this toxin, being inhaled or swallowed by, or otherwise introduced into man, produces in him a specific neuritis; and, just as man can carry the yeast plant from one place to another, so may he carry the beriberi germ.

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It is often remarked that when patients are removed from the endemic spots they at once begin to improve, and may be out of danger in a few days; whilst those who remain in the endemic area most probably go from bad to worse, and very likely die. It is as if the place were infected by the germ, and not the individual; else, why should patients begin to mend so rapidly after they leave the locality? It is as if some toxin were generated in the soil or surroundings, and, rising up, were absorbed day by day; but when the spot in which the toxin is generated is quitted, and there is no longer a constant renewal of the poisoning going on, the effects after a time steadily and gradually wear out. This is not what happens where a germ is parasitic in the human body and the direct cause of disease; in such circumstances disease and germ do not die out thus rapidly.

Hirota mentions a circumstance which powerfully supports this theory. Of fifty-two infants who suffered from beriberi while being wet-nursed by beriberic mothers forty-two recovered, five died, five were not accounted for. In the cases which recovered the improvement set in at once on the children being weaned. Had a germ operating inside the body been the cause of the symptoms, the germ and the disease it produced would not have died out so rapidly; but we can readily understand the cessation of symptoms on the supposition that they were caused by a toxin which, on the discontinuance of suckling, was no longer being imbibed.

Another argument in favour of this view lies in the fact that beriberi clings to certain ships, and that it is only when these ships get into warm latitudes or become artificially heated that the disease reappears, which it may do year after year. It is as if the germ, like that of some fungus, became dormant in cold and active in warm weather.

The germ viewed as being located in the body.—There are many circumstances in favour of this view, more especially, and apart from the analogy supplied by the vast majority of diseases whose causes are

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known, the fact that when introduced into a community beriberi may spread, its spread being greatly favoured by overcrowding.

Various opinions have been expressed as to where and how the germ operates after having thus obtained access to the body. Three principal views are advocated—(*a*) that, like the diphtheria bacillus, it has a special habitat (throat, Durham; gastro-intestinal mucosa, Hamilton Wright) where it distils its toxin; (*b*) that it lives in the blood; (*c*) that it lives in the contents of the intestinal canal. Our information specially bearing on any of these suggestions is far too meagre to justify anything approaching certainty. In none of these localities has the germ been definitely recognised. As regards the blood, it has been conclusively proved that in the established disease there is no cultivable bacterium.

Hamilton Wright advocates the hypothesis, long ago enunciated by Norman Chevers, that the neuritic element in beriberi stands in the same relation to a primary bacterial lesion—in this case a gastro-duodenitis—that the neuritis of diphtheria has to the throat lesion in that disease. Wright holds that the germ (a square-ended bacillus which he has found in a limited number of cases in the tissues) is derived from the fæces of beriberics, and resides in infected surroundings (floors, etc.); that it is taken in with soiled food, etc.; that after an incubation period of about ten days it produces a specific inflammation of the duodenal mucosa; that there the nerve-poison is evolved; that after about three weeks the duodenitis, and with it the active stage of neuronal poisoning, subside; but that the damaged nerves only slowly recover during what he calls the "beriberi residual" stage, which may persist for many months and be attended with the usual clinical fluctuations and dangers of a residual neuritis. In support of this view Wright adduces the observation that patients at the outset of their illness invariably (according to him) complain of loss of appetite, and of epigastric pain or discomfort, and that those who die in the early stage—first three weeks—of the disease invariably

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show injection, punctiform or more extensive hæmorrhages and swelling of the duodenal mucosa.

Considering the local, racial and climatic limitations of beriberi, there is some ground for the idea that the germ is protozoal, and that it may require an insect intermediary for its evolution and, it may be, introduction into the human body. Daniels, therefore, lays stress on the study of the blood in the earliest and even incubation stage of the disease, and on the insects associated with man in the tropics. He especially particularises lice, which have, he believes, racial predilections determined by their own antecedents; that is to say, a louse from a Chinese will prefer a Chinese; a louse from a Kling, a Kling, and so forth. Hence he suggests the peculiar immunity of the Kling. Mosquitoes, sand-flies and other biting flies need not be considered, as they are not present in at least one place where beriberi is not uncommon, namely, on ships. Besides lice, bugs and cockroaches must be taken into account.

In searching for the cause of beriberi it must be borne in mind that it is quite possible that several kinds of peripheral neuritis, each with its special cause, may in our ignorance have been included under the term beriberi, which, after all, may only be, like the word "dysentery," a name for a group of symptoms produced by several diseases of the same tissues or organs, and not of one special disease of these tissues or organs.

Morbid anatomy and pathology.—There is very little to be said about the *post-mortem* appearances in beriberi which is not covered by the accepted descriptions of the lesions of peripheral neuritis. There is a degeneration of the peripheral nerves—more especially of their distal ends, and there is secondary atrophic degeneration of muscle, including that of the heart, which may be the subject of an acute fatty degeneration like that of diphtheria. Hamilton Wright has recently shown that degenerative nerve changes (formerly denied) may be detected in the nerve centres and throughout the implicated neurons, as in other forms of peripheral neuritis. This observer seeks to correlate the early or "acute" phase of the disease with the primary poisoning of the nerve endings, the latter or "residual" phase with the stage of nerve degeneration. If there is anything peculiar about the *post-*

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mortem appearances in beriberi, it arises from the somewhat special implication of the central and peripheral organs of the circulation—namely, dilatation of the heart, especially of the right side, and great accumulation of blood in the right heart and in the veins. In addition, there is a marked liability in many cases to serous effusion into the pericardium, pleural cavities, peritoneum, and cellular tissue. This very marked liability to serous effusion, and the tendency to cardiac dilatation, may be said to be more or less distinctive of beriberic as compared with other forms of multiple neuritis. The type of œdema indicates that it depends especially on vasomotor disturbances, although cardiac weakness and partial suppresion of urine may be contributory elements. Œdema of the lungs also is not uncommon, and has, probably, a pathology similar to that of the connective tissue œdema. There is no nephritis. The only lesion that might be considered specific in beriberi is the duodenitis, which, according to Hamilton Wright, is invariably present in acute cases during the first three weeks of the disease. The invariableness of this lesion is denied by other observers—Daniels, Koch, and Hunter.

Mode of death.—The most practically important point in the pathology of beriberi is that which relates to the modes of death. The paresis and the atrophy of the voluntary muscles, the œdema of the connective tissue, and the serous effusions are, as a rule, not very serious matters—at all events as affecting life. But it is very different when paresis and degeneration seriously implicate the heart and the muscles of respiration. In nearly all beriberics there is heart trouble, arising, doubtless, from implication of the pneumogastric nerve and the cardiac plexus. In some patients the degree of implication is slight; but in others it is sufficient so to weaken the heart that death is inevitable. We cannot be quite sure in which cases the implication of the pneumogastric nerve or cardiac plexus is likely to be serious, or in which cases it is likely to be slight. Often the mildest cases of beriberi, as judged by the degree of voluntary muscle paresis or by the amount of œdema, are in reality the most dangerous. There appears to be an element of chance determining the nerves which the poison picks out. Sometimes one may see a case which is completely paralysed so far as legs and arms are concerned, and perhaps wasted to a skeleton; and yet this same patient may never have a serious symp-

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tom referable to his heart, or in any way threatening life. On the other hand, one may see a patient with very little paresis, very little œdema, and yet in a short time the heart may become involved, and he will die in a few minutes or hours. I presume the dilatation of the heart, the usual cause of death, is favoured or brought about by a concatenation of several conditions: by degeneration of muscle fibre following nerve destruction, by imperfect systole in consequence of an interrupted nerve supply, by obstruction to capillary circulation in consequence of vaso-motor paresis in the pulmonary and general circulation.

Once commenced, the cardiac dilatation tends to increase automatically; for the more the organ dilates, the more difficult does it become for it to contract, the greater the incompetency of the valves, and the more the blood stagnates in and over-distends it. The organ enters on a vicious pathological circle. Finally it becomes so distended that, like an overstretched bladder, it loses the power to contract altogether. The blood then rapidly accumulates in the great veins, the right auricle and ventricle are distended almost to bursting, and death is inevitable. The result is often contributed to by the co-existence of pleural effusion, hydropericardium, paresis of the diaphragm, over-distension of the stomach by food or gas, and, above all, by œdema of the lungs. It can readily be understood how the establishment of any additional obstruction of this description would still further tax the dilated, enfeebled heart, and determine the fatal issue.

When we come to make a *post-mortem* in these cases we may find a heart slightly hypertrophied and enormously dilated, the right cavities distended with blood, the lungs and liver full of dark blood, and all the great veins engorged.

Prognosis.—This tendency to dilatation of the heart is the dangerous element in beriberi; it should always be before our eyes, and dominate our plans of treatment. It is wonderful how rapidly it may come

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on, and how rapidly it may prove fatal. These sudden deaths, occurring sometimes from syncope—from instantaneous failure, as well as from the somewhat slower process of increasing over-distension, are constantly sprung on one in this disease. An absolutely favourable prognosis, therefore, ought never to be ventured on in even the mildest-looking case of beriberi, or so long as the patient is in the endemic area, or so long as the disease appears to be active. That is a lesson which is often, and sometimes painfully borne in on the practitioner in beriberi districts.

Evidences of grave heart implication, such as pulsating cervical vessels, equal spacing of the intervals audible on auscultation, enlargement of cardiac dulness especially to the right, epigastric pulsation, a rapid feeble pulse, a distended stomach, cold extremities, cyanosis, dyspnœa, and a disproportion in the strength of the heart- and wrist-beats, are significant of danger. *Paralysis of the diaphragm, of the intercostal muscles, extensive serous effusions, very scanty urine* are also unfavourable signs.

Vomiting.—No one can say when or how soon fatal implication of the pneumogastric and other cardiac nerves may take place, but vomiting is always an ugly and threatening symptom in beriberi; it probably indicates that the former important nerve is being attacked. The Japanese regard the occurrence of vomiting as of fatal import. Marked dilatation of the stomach has a similar significance.

Prognosis is improved if the patient is early removed (that is before the heart muscle, or the cardiac or respiratory nerves, are gravely degenerated) from the place in which the disease was contracted to a healthy, non-beriberic, high-lying locality.

Mortality.—The mortality in beriberi varies in different epidemics and in different localities. On the whole, it is greater in low than in high latitudes, in the dropsical than in the atrophic forms, in the acute than in the chronic. In some epidemics it is as high as 30 per cent. of those attacked; in others as low as 5 per cent., or even lower.

Diagnosis.—Usually the diagnosis of beriberi is

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not difficult. Multiple peripheral neuritis occurring as an epidemic, or in a place or ship in which the disease has occurred on some previous occasion, may as a rule be set down as beriberi. Sporadic cases may be difficult to diagnose, more especially if there is a history of alcoholism, malaria, or of drugging with arsenic. The presence, actual or past, of œdema—especially of œdema over the shins—and palpitations and other evidences of cardiac implication, are significant of beriberi. It must be borne in mind that slighter degrees of beriberic poisoning, evidenced only by slight anæsthesia of the pretibial skin area, by slight œdema of the same region, by slight hyperæsthesia of the calf muscles, and, perhaps, by impairment or absence of knee-jerk, may be the only symptoms present. True rheumatism is rare in the tropics. Among natives, especially if their language is not understood, complaints of what may seem to be rheumatic pains in the legs should always be carefully investigated, the knee-jerks tested, and signs of hyperæsthesia of the calf muscles sought for. The significance of these signs of what may be described as larval beriberi is too frequently overlooked until some sudden death, which, with earlier recognition of the disease, might have been avoided, puts the practitioner on his guard. All paretic affections, all cases of œdema, all cases of palpitation, and all cases of rheumatic-like pains occurring among the natives of warm climates, therefore, should suggest the possibility of their being beriberic, and also the necessity for a detailed examination with this in view.

Treatment.—The first and most important thing to be attended to in the treatment of a case of beriberi is the removal of the patient from the building, camp, or ship in which the disease was contracted. His condition warranting transport, if possible the patient must be got out of the endemic spot.

He should be removed to some dry locality and, if such is available, sleep well off the ground in a thoroughly ventilated, sunny room situated in an upper storey. He ought to clothe sufficiently and feed well,

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taking care that the food is not of a bulky character, and that it contains a sufficiency of nitrogenous and fatty elements. Rice is found to be a bad food for beriberics; it is too bulky. Wheaten flour is better, so is oatmeal. Beans of different kinds seem specially suitable for these cases; they are cheap and contain much nitrogenous matter in relatively small compass. Animal food, including fat, must enter into the dietary in reasonable amount. Milk and eggs are beneficial. The worst cases, particularly if there is any sign of serious cardiac implication, should remain in bed; but the mild cases had better spend the greater part of the day in the open air. If the disease break out on shipboard, the dietary should be changed and the crew should be kept out of the forecastle, and, so far as possible, made to sleep on deck, properly protected from the weather by an awning.

With a view to diminishing to some extent the bulk of blood in the vessels and heart, the seriously affected patients should take little fluid, and keep the bowels free by some saline aperient. In cardiac cases small doses of digitalis or of strophanthus seem to do good. Should signs of acute cardiac distress appear, full doses—three, four, or five drops of the 1 per cent. solution—of nitro-glycerine are indicated. This must be repeated every quarter or half hour, and kept up until the threatening symptoms pass away. In suddenly developed cardiac attacks inhalations of nitrite of amyl, pending the operation of the nitro-glycerine, may be given. It is well for these two drugs to be in the hands of properly instructed ward attendants, so as to meet cardiac complication on its earliest appearance. There is often no time to send for the doctor. Should signs of cardiac distension and failure persist and increase, in spite of these means, there must be no hesitation in bleeding the patient, taking, if it will flow, eight or ten ounces from the arm, or, this failing for any reason, from the external jugular. Often, as the blood flows, rapid amelioration of the alarming condition sets in, and the patient is, for the time being, tided over an acute danger and given another chance.

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The bleeding should be repeated if the alarming symptoms recur, as they are almost sure to do. Oxygen inhalations, if available, are worth trying in cardiac attacks. Pleural and pericardial effusions should be sought for, and, if deemed to be interfering in the slightest degree with the circulation or respiration, drawn off with the aspirator.

Provided the patient has been removed from the spot where he was being poisoned, and provided he can be tided over the first fortnight, he will probably recover; but in a serious case, should he remain in the place where his disease was acquired, though he may get over one or two cardiac attacks, the risk to life in bad epidemics is very great indeed, and he will almost surely die.

For the atrophy of the muscles and anæsthesia of the skin, faradisation and massage are of service, and should be employed so soon as the muscular hyperæsthesia has begun to subside. Strychnine, arsenic, and nitrate of silver are in repute as tonics in these circumstances. Care should be taken that permanent deformity does not occur from contraction of muscles. Foot-drop should be counteracted by Phelps's talipes splint with an elastic accumulator, and any other threatened deformity appropriately met. Relapses must not be risked by a return to the original source of infection. The seaside or a sea voyage has often a marvellously restorative effect.

When beriberi breaks out in a school, gaol, or similar institution the place should be emptied of its inmates as soon as possible; at all events, those parts of the building in which the disease has appeared ought to be cleared out and not reoccupied until they have been thoroughly cleansed, disinfected, ventilated, and dried. Overcrowding must be strictly avoided. Ventilation must be effective. The dietary should be revised and, if necessary, have rice eliminated from it as much as possible; in the place of rice, meat, flour, or beans should be substituted. All the inmates should be obliged to pass the largest part of every day in the open air; their knee-jerks should be

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tested, and their legs examined for numbness, œdema, and muscular hyperæsthesia from time to time. Any suspicious case should be removed at once.

Should beriberi appear on board ship, besides the precautions already indicated, special means of disinfection must be employed. Rotten planking and bilge-water must be removed from the neighbourhood of the quarters of the crew; the sound woodwork should be scraped and painted; disinfectants should be freely and frequently employed, clothes and sea-chests washed and disinfected, and every means necessary to destroy lurking germs vigorously adopted.

In beriberi countries low-lying, damp situations should be avoided as building sites. The sleeping quarters, especially, should be raised well off the ground, and located, if possible, in an upper storey; all rooms should be so arranged as to be easily flushed with fresh air and flooded with sunlight.

As yet we know neither the virus of beriberi nor the way in which it is acquired. It is certainly communicable, and until we have more precise knowledge it is unjustifiable not to recognise the subjects of the disease as being possible sources of danger to others. Therefore, in the endemic zone, that is to say, where the virus may encounter the conditions it requires for successful passage from man to man, beriberics should be treated as infective and should be isolated. In gaols and similar institutions newcomers, whether manifestly suffering from beriberi or not, should be isolated and kept under special observation for a time, their clothes disinfected and their body vermin scrupulously destroyed. Prison clothes and prison blankets especially should invariably be disinfected before being passed into store and before being served out. The utmost care should be exercised to keep prisoners free from vermin and the premises from flies, cockroaches, fleas, bugs and all insects that might possibly serve as transmitters of the virus.

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CHAPTER XXV

EPIDEMIC DROPSY

Definition and description.—A specific, epidemic, communicable disease running its course in from three to six weeks, and characterised by the sudden appearance of anasarca, preceded in most instances by fever, vomiting, diarrhœa, or by irritation of the skin, and often accompanied by a rash, by fever of a mild, remitting type, by disorder of the bowels, and by pronounced anæmia. The case mortality varies from 2 to 40 per cent., death being sudden and depending upon œdema of the lungs, hydrothorax, hydropericardium, or other pulmonary and cardiac complications.

History and geographical distribution.—The foregoing is a concise description, drawn principally from McLeod's account (*Trans. Epidem. Soc. Lon., N.S.*, vol. xii.) of a disease which appeared in Calcutta, it is believed for the first time, in the cold weather of 1877–78, of 1878–79, and 1879–80. On each occasion it disappeared with the advent of the hot weather. The same disease broke out at Shillong, Assam, 5,000 feet above the level of the sea, in October, 1878; at Dacca in January, 1879; at South Sylhet in the cold weather of 1878–79; and in Mauritius (Lovell and Davidson), having been imported from Calcutta, in November, 1878. There are no trustworthy accounts of its occurrence elsewhere, although certain vague statements seem to indicate that it appears at times in other parts of India. In Mauritius it prevailed until June, 1879, attacking about one-tenth part of the coolie population, of whom 729 died, a mortality of about 2 or 3 per cent. At Sylhet there were no deaths; at Shillong also the mortality was insignificant; but in Calcutta the death-rate in those attacked was estimated as high as 20 to 40 per cent. Coolies and

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natives were alone affected; Europeans enjoyed a complete immunity. In Calcutta the disease was confined to a particular quarter; here it attacked families and groups of people, slowly extending its area, but at no time becoming generally epidemic throughout the city. A very limited epidemic of the disease appeared again in Calcutta in 1901.

Ætiology.—Both sexes were attacked; children under puberty were less liable than adults; sucklings were seldom affected. The weak and the robust were equally susceptible. There are no direct observations on the germ of the disease; there is distinct though indirect evidence of its portability and of its communicability. But as to whether it is directly communicable from man to man, or whether it, or its product, is indirectly transmitted through some unrecognised medium has not been determined. Evidence of its capacity for remaining latent for a considerable period is supplied by the history of the successive epidemics in Calcutta. The disease could not have been a very catching one, seeing that no medical man was attacked, and that, except in the case of Mauritius, it spread but slowly.

Identification.—McLeod, after a careful analysis of all the available evidence, concludes that epidemic dropsy is a disease *sui generis*. At the time of its occurrence in Calcutta many of the physicians there looked upon it as a form of beriberi; and, indeed, in many respects it resembles very closely those cases of beriberi in which dropsy is a prominent symptom, and in which the nervous phenomena are slight or altogether absent. But in epidemics of beriberi such cases are the exception—in fact, are very rare, and always concur with others in which nerve symptoms are pronounced, and with purely atrophic cases; such were not seen in either the Calcutta or the Mauritius epidemics. In epidemic beriberi the mortality is much higher than in the Shillong or in the Sylhet epidemic. Furthermore, beriberi is a much more chronic disease, is not accompanied by an eruption, and but seldom with well-marked fever.

Special symptoms.—According to McLeod

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dropsy was almost invariably present. It usually appeared first in the legs, and in some instances was confined to the lower extremities; in others it spread and involved the entire body. Occasionally it was very persistent, lasting and recurring during convalescence.

Fever also was a very constant symptom; sometimes it preceded, sometimes it accompanied, sometimes it succeeded the dropsy. It was rarely high, ranging usually from 99° to 102°; in a few cases—possibly from malarial complications—it reached 104°. Rigors were rare.

Diarrhœa and vomiting generally ushered in the disease in the Mauritius epidemic. In Calcutta these symptoms were not so frequent, although they were by no means rare there, occurring at both the earlier and later stages. Dysentery was common in the Calcutta epidemic.

Nervous symptoms—such as burning, pricking, itching, and feelings of distension of the skin, sometimes limited to the soles and feet—often preceded the dropsy. Distressing aching of muscles, bones, and joints, worst at night, was usual. Anæsthesia of skin areas and paresis of muscles were never observed in Mauritius. Harvey remarked two cases in Calcutta exhibiting doubtful paretic symptoms; these are the only two recorded in which there was anything resembling the paretic symptoms usually so prominent a feature in beriberi.

An *exanthem*, erythematous on the face, rubeolar on the trunk and limbs, was frequently seen in Mauritius, less frequently in Calcutta. It appeared about a week after the œdema, and lasted from ten to twelve days.

Circulation and respiration.—Disturbances of the heart and circulation were prominent features in nearly all the cases. The pulse was weak, often rapid and irregular; cardiac bruits were also noted. Breathlessness on exertion occurred in all cases; severe orthopnœa in many. Signs of pleural and pericardial effusion, of œdema of the lungs, of pneumonia, and of cardiac dilatation were common in Calcutta.

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Anæmia was usually present and marked; so were wasting and prostration. Scorbutic symptoms occasionally showed themselves.

The *liver, spleen and kidneys* were not specially affected. The urine was rarely albuminous.

Morbid anatomy.—Beyond general œdema and occasional pleural and pericardial effusion, nothing special was remarked *post-mortem*.

Treatment.—In the absence of anything like precise knowledge of the cause and pathology of epidemic dropsy, treatment must be entirely symptomatic. Mild purgatives, the exhibition of digitalis when there is evidence of cardiac weakness, and the occasional use of the nitrites in the fits of orthopnœa might prove serviceable. During convalescence iron and arsenic are indicated.

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SECTION III.—ABDOMINAL DISEASES

CHAPTER XXVI

CHOLERA

Definition.—An acute, infectious, epidemic disease, characterised by profuse purging and vomiting of a colourless serous material, muscular cramps, suppression of urine, algidity and collapse, the presence of a special bacterium in the intestine and intestinal discharges, and a high mortality.

History and geographical distribution.—It is probable that from remotest antiquity cholera has been endemic in Lower Bengal,* and that thence, from time to time, it has spread as an epidemic over the rest of India. European physicians observed it there in the sixteenth, seventeenth, and eighteenth centuries, but it was not until the great epidemic extension of 1817 that the disease seriously attracted the attention of the profession in Europe. In that year cholera began to spread all over Asia, extending eastwards as far as Pekin and Japan, southwards to Mauritius, and westwards to Syria and the eastern shores of the Caspian. Stopping short at Astrakhan in 1825, it did not on that occasion invade Europe.

European epidemics.—In 1830 cholera visited Europe for the first time. Advancing through Afghanistan and Persia, it entered by way of Russia, and swept as an epidemic over nearly the entire continent, reaching Britain at the beginning

* Though it is customary to speak of Lower Bengal as the home of cholera, it is by no means certain that other Eastern localities have not some claim to a similar distinction—Bankok, Canton, and Shanghai, for example. Dr. Henderson, in his health reports, indicates that the disease is rarely absent during the summer months from the last-named city; the same may be said of Bankok and of Canton.

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of 1832. During the same summer it crossed the Atlantic to Canada and the United States. This epidemic did not die out in Europe till 1839. Since that time there have been at least five European epidemics—1848–51, 1851–55, 1865–74, 1884–86, and 1892–95.

Great Britain has been seriously involved in four only of these epidemics—namely, in 1832, 1848, 1854–55, and in 1866. On the occasion of the last two European epidemics, although the disease was frequently imported, it did not spread in Britain. America has not been so fortunate, for, although the 1870–73 epidemic practically spared Great Britain, it crossed the Atlantic and, entering by way of Jamaica and New Orleans, raged for a time in the United States.

From a study of the march of these various epidemics, it is to be concluded that cholera reaches Europe by three distinct routes:—*First*, viâ Afghanistan, Persia, the Caspian Sea, and the Volga valley; *second*, viâ the Persian Gulf, Syria, Asia Minor, Turkey in Europe, and the Mediterranean; and, *third*, viâ the Red Sea, Egypt, and the Mediterranean.

With certain exceptions, hereafter to be mentioned, there is hardly an important country in the world which has not, at one time or another, been visited by cholera in the course of some of its pandemic extensions.

Ætiology.—*The disease is carried by man.*—The study of the various epidemics shows that in its spread cholera follows the great routes of human intercourse, and that it is conveyed chiefly by man, probably in its principal extensions by man alone, from place to place. In Britain and the United States, for example, the places first attacked have been invariably seaports in direct and active communication with other ports already infected. In India, although the problem is much more difficult to unravel, in certain instances the influence of human intercourse in diffusing the disease can be distinctly traced. Thus the extensive pilgrimages, so frequent in that country, are a fruitful source of its rapid spread. During these gatherings hundreds

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of thousands of human beings are collected together under highly insanitary conditions—as at the Hurdwar and Mecca pilgrimages. Cholera breaks out among the devotees, who, when they separate, carry the disease along with them as they proceed towards their homes, infecting the people of the places they pass through. Cholera never travels faster than a man can travel; but in modern times, owing to the increased speed of locomotion and the increased amount of travel, epidemics advance more rapidly and pursue a more erratic course than they did sixty years ago.

Isolation secures immunity. — In the case of isolated countries the absence of active and frequent intercourse with the outer world favours immunity, even during approximately pandemic extensions. Thus, though so near to the reputed home of cholera, the Andaman Islands have never been visited by that disease. Similarly, Australia and New Zealand hitherto have enjoyed practical exemption. The same can be said of the Pacific Islands, the Cape of Good Hope, the west coast of Africa, Orkney and Shetland, Iceland, the Faröe Islands, and many of the islands of the Atlantic.

Its unequal diffusion in the endemic and epidemic areas.—Although cholera is always present in some part of the endemic area in Bengal, it is not equally diffused there, nor is it equally common at all seasons and every year. Thus, even within this area, there are places which enjoy an absolute or a relative immunity, and there are seasons and years of special prevalence. It has also to be remarked that the season of immunity for one place may be the season for prevalence in another place, and *vice versâ*. The same observations apply to the areas of epidemic extension.

When cholera extends as an epidemic, its course is often singularly erratic. Some places, apparently in the direct line of advance, are passed over, to be attacked perhaps at a later period. Similarly, certain districts of a town may be spared, while other parts of the same town are ravaged by the disease.

Local conditions favouring its presence.—On the whole, it may be said that low-lying districts,

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particularly those along the banks of rivers, are more subject to the disease than high and dry situations; and that overcrowding and unhygienic conditions generally conduce to its prevalence. The principal and special element, however, which determines the diffusion of cholera is, undoubtedly, the character of the water supply.

Cholera in the main a water-borne disease, entering by the stomach.—From time to time many theories of the cause and nature of cholera have been put forward, most of them very absurd and manifestly incorrect. Most of these have now been definitely abandoned in favour of the theory that the cause of cholera is a specific germ which, in the main, is water-borne. The evidence in favour of this view may be regarded as being almost conclusive, although there is still some room for doubting whether the germ itself has really been discovered.

The earliest, and still one of the most telling pieces of evidence in favour of the water-borne theory of the diffusion of cholera, we owe to the late Dr. Snow. In August, 1854, cholera was epidemic in parts of London, notably in the neighbourhood of St. Anne's, Golden Square. A child, after an illness of three or four days, died of the disease at 40, Broad Street, on the 2nd of September. The discharges from the patient had been thrown into a leaky cesspool which, as was subsequently discovered, drained into a well only three feet away. This well supplied the neighbourhood with drinking-water. On the night of the 31st of August cholera broke out among those who used the water of this particular well, very few escaping an attack. On the 2nd of September a lady died of cholera at Hampstead. Attention was specially called to this lady's case, as hitherto the disease had not been seen in that district. On inquiry it was found that she had been habitually supplied with drinking-water from the Broad Street well referred to, as she had formerly resided in Broad Street, and had retained a liking for the water from this particular well. She drank some of the water which had been procured on the 31st of August,

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both on that day and again on the 1st of September. On the latter day she was seized with cholera. A niece, on a visit to this lady, also drank some of the same water; she, too, was attacked by cholera, and died. A servant also drank the water; although she suffered to some extent, she recovered. So far as could be ascertained by careful inquiry, these people had had no connection whatever with the cholera district except through the water fetched from this particular Broad Street well. Cholera, as mentioned, was not epidemic at Hampstead at the time. The inference that the germ had been conveyed in the polluted water is difficult to avoid.

Another remarkable illustration of the diffusion of the cholera germ by water is supplied by a recent epidemic in Hamburg. At the time the sanitary conditions under which the inhabitants of the contiguous cities of Hamburg, Altona, and Wandsbeck lived were practically identical, save in the matter of water supply. Hamburg and Altona both drew their water from the Elbe; but, whereas the water distributed to the people of Altona was most carefully filtered, that supplied to the people of Hamburg was simply pumped up from the river and passed directly into the mains without filtration or purification of any description. The Wandsbeck water came from a lake, and was filtered. In Hamburg, during the epidemic, there were 8,605 deaths from cholera, equal to 13·4 per thousand; whereas in Altona only 328 deaths occurred, equal to 2·1 per thousand. The death-rate in Wandsbeck was similar to that of Altona. Hamburg and Altona are contiguous, and practically one city. At one part a street forms the boundary between the municipalities. On one side of this street, the Hamburg side, there were numerous cases of cholera; on the Altona side there were no cases. The houses on both sides of the street were of the same character and occupied by the same class of people. The only difference, so far as could be ascertained, was in the water supply: the houses on the healthy side of the street received Altona water; those on the cholera-stricken side, Hamburg water.

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It was remarked that a certain group of houses on the Hamburg side remained free from the disease. On investigation it was found that, unlike the other houses on the same side, these houses derived their water supply from an Altona main.

As regards its relation to the water supply, this Hamburg epidemic is the exact counterpart of what happened in South London in 1854. Formerly this district was supplied with water by two companies—the Southwark and Vauxhall Company and the Lambeth Company. Both companies drew their water from the Thames—the latter from near Hungerford Bridge, the former from near Battersea Fields. The epidemic of cholera which visited London in 1849 was especially severe in South London. Subsequently the Lambeth Company removed its intake higher up the river to Thames Ditton, and consequently the water it supplied at the time of the 1854 epidemic had improved in quality. The Southwark and Vauxhall Company did not change their intake, and in 1854 they were still drawing their supply from the river near Battersea Fields. When cholera visited London in that year the death-rate from the disease in the houses supplied by the Southwark and Vauxhall Company amounted to 153 per 10,000 inhabitants, whereas that in houses supplied by the Lambeth Company was only 26 per 10,000. The mains of the two companies ran side by side, some houses receiving the water of one company, some that of the other.

During the Hamburg epidemic it was also found that the incidence of cholera was three times greater among those who used the town water than among those who got their supplies from wells. These, and many similar facts which might be adduced, clearly point to water as a principal medium for the diffusion of the cholera germ.

The virus contained in the dejecta.—Evidence equally conclusive tends to show that the germ on being swallowed by man multiplies in his alimentary canal, and, on being voided in the dejecta, subsequently finds its way by a route more or less direct to water again, in which, under favourable

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conditions, it continues still further to multiply. An illustration, amounting almost to proof, of the fact that the germ of cholera is contained in the stools of cholera patients is supplied by Macnamara. Some of the characteristic rice-water discharge from a cholera patient got mixed accidentally with a few gallons of water. This was exposed to the sun for twelve hours. Early the following morning nineteen persons each drank about an ounce of the mixture. Within thirty-six hours five of these nineteen persons were seized with cholera.

Conditions of infection are complex.—It is evident that the ingestion of the germ is a necessary condition for the production of the disease, but there are many facts which render it equally evident that this is not the only condition. Were it the only condition, then every one of those individuals referred to by Macnamara would have sickened. What the other necessary conditions may be it is in the present state of knowledge impossible to say.

There is reason to believe that not only are the conditions complicated as regards the susceptibility of the individual, but also that they are equally complex as regards the germ itself in relation to its pathogenic, proliferating, and diffusing properties.

The germ of cholera.—*Early views.*—Since European pathologists first directed their attention to the subject, many views have been entertained as to the exact nature of the cause of cholera. Some of these views were of the most fantastic description. Mysterious atmospheric and telluric conditions were invoked, and only a very few years ago superstitious notions worthy of the Middle Ages were freely ventilated, even in high places and by educated minds. Among those who ventured to formulate definite and more reasonable hypotheses some considered that cholera, like the more familiar exanthematous fevers, was directly contagious. Others thought that it was not directly contagious, but that it was communicated by the evacuations of the sick after these evacuations had undergone some peculiar fermentation process outside the human body. Others, again, as Von Petten-

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kofer, regarded the virus as a chemical ferment which developed in the soil under certain unknown epidemic conditions.

Discovery of the comma bacillus.—Since the rise of the germ theory of infective disease most of these speculations have been definitely abandoned, or have received more precise expression in the view that cholera is caused by a certain bacterium, known as the comma bacillus or cholera vibrio, which Koch found to be present, practically invariably, in the stools and intestinal contents of cholera patients. This bacterium Koch first discovered in Egypt in 1883. Believing in its importance, he afterwards proceeded to India on a special mission and there, in Calcutta, in 1884, he found the same bacterium in the intestinal contents of forty-two fatal cases, and in the stools of thirty other cholera patients; in fact, he found it in every case of the disease examined. Moreover, he entirely failed to find it in any other disease or in healthy discharges. These observations, so far as they concern the presence of the comma bacillus in cholera stools, have been abundantly confirmed by many other workers; so that the presence or absence of this bacterium is now regarded as a trustworthy and valuable practical test of the choleraic or non-choleraic nature of any given case of intestinal flux; and this even by the opponents of Koch's special view as to the nature of the relationship of the bacterium in question to the disease with which it is so intimately associated. If only on account of its diagnostic value, the comma bacillus, therefore, is an organism of importance; but as many high authorities regard it as a necessary concomitant and even as the actual germ and true cause of Asiatic cholera, the vibrio acquires an importance of the first rank.

Description of the comma bacillus.—The comma bacillus (Fig. 60) is a very minute organism, 1·5 to 2 μ in length by ·5 to ·6 μ in diameter—about half the length and twice the thickness of the tubercle bacillus. It is generally slightly curved, like a comma; hence its name. After appro-

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priate staining, at each end, or at one end only, flagella can be distinguished; sometimes one, sometimes (though less frequently) two. These flagella, though of considerable length—from one to five times that of the body of the bacterium, owing to their extreme tenuity are difficult to see in ordinary preparations. They are not always present during the entire life of the parasite. In virtue of this appendage the bacillus exhibits very active spirillum-like movements. The individual bacilli when stained

Fig. 60.—Cholera bacillus. Agar culture: 24 hours' growth. (× 1000.) (*Muir and Ritchie.*)

show darker parts at the ends or at the centre, suggesting spore formation. Sometimes in cultivations two or more bacilli are united, in which case an S-shaped body is the result; or it may happen that several bacilli are thus united together, producing a spirillar appearance.

The comma bacillus is easily stained by watery solutions of fuchsin, or by Löffler's method, dried cover-glass films being used. Dilute solution of methyl violet mixed with the intestinal contents and placed on a slide suffices for partial staining.

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The bacillus grows best in alkaline media at a temperature of from 30° to 40° C. Growth is arrested below 15°, or above 42° C.; a temperature over 50° C. kills the bacillus. Meat-broth, milk, blood serum, nutrient gelatine, or potato, are all suitable culture media. Nutrient gelatine and potato are the most convenient for diagnostic purposes.

In gelatine plate-cultivations minute white points appear; around these the gelatine liquefies, and the colonies of bacilli sink into funnel or bubble-shaped depressions. By the end of the second or third day the cultivation is besprinkled with such depressions, liquefaction spreading peripherally until it involves the entire surface of the gelatine. The colonies are white or yellowish, very irregular in shape, granular, and shining like so many particles of ground-glass. Later they assume a peculiar roseate hue, said to be absolutely characteristic.

In gelatine stab cultures the growth at first is most active near the surface; later, the colony sinking, liquefaction advances most below the surface of the gelatine, so that a bubble-shaped appearance is produced. Later still, as growth proceeds along the needle track, a finger-shaped liquefaction results, which in time extends to the sides of the tube. At the bottom of the liquefied area there is an accumulation of a white mass of bacteria; at the top a scum of bacteria in various stages of degeneration. The cultures may die after five or six weeks.

Agar is not liquefied, and in it the cultivations retain their vitality longer. On potato, at 20° to 30° C., the culture appears as a thin, brownish, porcelain-like film. In broth, some of the bacilli form a scum on the surface; others, falling in masses to the bottom, leave the body of the liquid clear.

Although, taken together and in conjunction with the morphological appearances, these culture characters are fairly distinctive, nevertheless certain other bacteria, such as Finkler's spirillum, behave very similarly; and, as the microscopic features of those other bacteria in some instances are very much like that of the cholera vibrio, a mistake is easily made.

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The production of what is known as "cholera red" by the addition of pure sulphuric acid (indol reaction) to a culture in peptonised broth, is also not quite distinctive of the cholera vibrio, for a similar reaction is produced by some other bacilli.

In careful and practised hands the diagnosis of cholera by the microscopic and cultural characters of the vibrio may be made with practical certainty.

Is the comma bacillus the germ of cholera?—Although it may be safely asserted that cholera is intimately associated with the comma bacillus, it does not necessarily follow that this organism is the cause of cholera. Many attempts have been, and are being made to establish such a relationship. Nevertheless, what may be considered as absolute proof is still wanting; such proofs as alone can be afforded by the production in man, or in the lower animals, of a disease in every respect like cholera by the administration of pure cultures of the comma bacillus. Short of this the proof may be said to be almost complete; indeed, by not a few the causal relationship of the bacillus to the disease is considered as established.

Since Koch first announced his discovery many facts having a bearing on the subject have been brought to light, some in favour of his views, some apparently militating against them.

(1) It has been found that there are several bacilli with morphological and cultural characters closely resembling those of the cholera comma, notably the Finkler-Prior bacillus of cholera nostras, Lewis's saliva comma bacillus, many of the comma-shaped bacilli discovered by Cunningham, and certain species found in river water. Koch and others maintain that, though morphologically similar, as these various bacilli behave so differently from that of cholera in culture media, they must be considered as biologically specifically distinct from the latter.

(2) Cultures of pure bacilli have many times been swallowed by way of experiment; yet, although in some instances diarrhœa with comma bacilli in the stools has resulted, in only a very few instances has true cholera been produced. On this account

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it is held by some that the comma bacillus cannot be regarded as the germ of cholera. Against this it is advanced that other factors must be present to insure the induction of cholera by such experiments; for example, a suitable and peculiar condition of the body, possibly, as Buchner suggests, some second and as yet unknown micro-organism. Buchner accordingly regards cholera as the result of a mixed infection. It is to be presumed, therefore, that in the two or three instances in which cholera followed on the intentional or accidental ingestion of cultures of the cholera vibrio, these secondary but essential conditions were present. It must be remembered also, in assessing the value of negative feeding experiments, that the cholera vibrio, like other pathogenic bacteria, may lose through cultivation, or otherwise, its virulence while retaining its morphological and cultural qualities.

(3) A few cases of what, from a clinical point of view, appears to be true cholera have been observed in which the most careful and most prolonged bacteriological examinations failed to detect the comma bacillus. Therefore, it has been advanced, as cholera can occur without the comma bacillus, the comma bacillus cannot be the cause of cholera. Against this it has been said that these observations were defective; that although the bacillus was not found, it by no means follows that the bacillus was not present at some time in the case.

(4) The comma bacillus has been observed in the stools of individuals who did not at the time or afterwards suffer from cholera. To this it is answered that although one of the necessary conditions for the production of cholera was present, others, equally necessary, were absent. Possibly, as Pettenkofer remarked, for the production of an attack of cholera three things might be necessary, X, Y, and Z. The comma bacillus may be the X, but in the absence of the Y, certain local, and of the Z, certain personal conditions, disease does not result.

(5) It has been found impossible by the administration of comma bacilli to produce in the lower animals

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true cholera, or any condition with clinical symptoms closely resembling cholera. Koch and others, in certain experiments on guinea-pigs, acting on the supposition that the acid in the stomach killed the bacillus, neutralised this by the administration of sodium carbonate, and paralysed the intestine by intraperitoneal injections of tincture of opium. In this way they claim to have succeeded in killing guinea-pigs with symptoms to a certain extent like those of cholera. There are many sources of fallacy in this experiment, as has been pointed out by Klein and others. Exactly similar results can be got by using the Finkler-Prior and other bacilli. The most promising experiments in this direction are those by Jablotny on the ground squirrel, *Spermophilus guttatus*. By administering to this animal comma cultures in alkaline media a disease in many respects like cholera was produced; and, in the intestines and discharges of the animals experimented on, cholera-like pathological changes were found, as well as comma bacilli.

Variability of the cholera microbe. — Bacteriological studies, always difficult, are extremely so in the case of the cholera microbe owing to its special liability to variation, both in its morphological and in its pathogenic characters. On this subject Haffkine remarks: "When the cholera bacillus was first discovered its properties were described with extreme precision, which helped in concentrating for a long time all studies on well-defined and carefully chosen specimens. Little by little, as the field of observation grew larger, a number of varieties have been found with characteristics differing so largely as to annihilate almost completely the original description. When we open the intestine of deceased cholera patients and investigate the microbes there, the adopted methods will bring to the surface vibrios in which the external forms, instead of the characteristic comma or spirillum, will vary between a coccus and a straight thread; the number and disposition of the cilia, the secretion of acids, the form of growth in broth, will vary; instead of giving in gelatine a discrete and well-defined figure of liquefaction, the variation will extend from the

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complete loss of this property to a rapid dissolution of the whole medium; there will be varieties which grow luxuriantly in given media, and others which do not grow there at all; some will be phosphorescent in the dark, and others not; some will give the indol reaction, and others will be deprived of this property, and so on. The first thing to be done is to select carefully among these the most typical specimens, rejecting the others, and then to try their pathogenic power. We shall find such a divergence in strength that the extreme forms will not be believed to be the cholera species. There will be commas deprived of any virulence demonstrable on animals, and others which will kill the most resistant species. Some will be fatal to a guinea-pig at a dose of $\frac{1}{100}$ of a culture tube, and others harmless in doses 500 times stronger. The average comma dies out when introduced under the skin of an adult animal; others will spread in the system and give rise to a fatal septicæmia. The ordinary comma will be without effect on birds; but several specimens have been isolated, and believed to be typical, which easily killed pigeons by hypodermic or intramuscular injection. I believe to be of great value the method worked out by Pfeiffer for comparing all such varieties with one selected as typical, which he employed for the preparation of an antitoxic serum. This method will be found of efficient help in distinguishing specimens of the greatest affinity with the average cholera comma. But once such specimens are selected and their particular properties studied they begin to change from the first day they are introduced into the laboratory, and no calculation based on these studies is possible. In a case quoted by M. Metchnikoff, the proportion of the initial power of the microbe, and the strength it showed at a later trial, was as 75 to 1, the microbe having gradually sunk to $\frac{1}{75}$ of its initial virulence." These remarks, by so great a master of the subject, whilst they indicate a way of reconciling many apparent discrepancies in matters of fact and differences in the conclusions arrived at by different bacteriologists, and whilst they indicate a key to many of

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the clinical features of cholera, teach us caution in accepting as proved the causal relationship of the cholera vibrio to the disease with which it is so invariably associated.

Symptoms.—An attack of cholera commences in one of two ways: either it may supervene in the course of what appears to be an ordinary case of diarrhœa, or it may come on suddenly and without any well-marked prodromal stage. During cholera epidemics diarrhœa is unusually prevalent. It is a common observation that at such times an attack of this latter nature, after a day or two, may assume the characters of true cholera. The preliminary looseness in such cases is called the "premonitory diarrhœa." Whether this looseness is specifically related to the subsequent attack, or whether it is of an ordinary catarrhal or bilious type and acts simply by predisposing to the specific disease, has not been determined. Possibly, owing to a catarrhal condition—in itself non-specific—the resisting power of the mucous membrane is impaired; possibly, in diarrhœa, the large amount of fluid in the gut affords a favourable medium for the cholera germ to multiply in. Besides diarrhœa, other prodromata, such as languor, depression of spirits, noises in the ears, etc., are sometimes noted.

When true cholera sets in, profuse watery stools, painless or associated with griping, and at first fæcal in character, pour, one after the other, from the patient. Quickly the stools lose their fæcal character, becoming colourless or, rather, like thin rice water containing small white flocculi in suspension. Enormous quantities — pints — of this material are generally passed by the patient. Presently vomiting, also profuse, at first perhaps of food, but very soon of the same rice-water description, supervenes. Cramps of an agonising character attack the extremities and abdomen; the implicated muscles stand out like rigid bars, or are thrown into lumps from the violence of the contractions. The patient may rapidly pass into a state of collapse. In consequence principally of the loss of fluid by the diarrhœa and vomiting, the soft

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parts shrink, the cheeks fall in, the nose becomes pinched and thin, the eyes sunken, and the skin of the fingers shrivelled like a washerwoman's. The surface of the body becomes cold, livid, and bedewed with a clammy sweat; the urine and bile are suppressed; respiration is rapid and shallow; the breath is cold and the voice is sunk to a whisper. The pulse soon becomes thready, weak, and rapid, and then, after coming and going and feebly fluttering, may disappear entirely. The surface temperature sinks several degrees below normal—to 93° or 94° F.; whilst that in the rectum may be several degrees above normal—101° to 105° F. The patient is now restless, tossing about uneasily, throwing his arms from side to side, feebly complaining of intense thirst and of a burning feeling in the chest, and racked with cramps. Although apathetic, the mind generally remains clear. In other instances the patient may wander or may pass into a comatose state.

This, the "algide stage" of cholera, may terminate in one of three ways—in death, in rapid convalescence, or in febrile reaction.

When death from collapse supervenes, it may do so at any time from two to thirty hours from the commencement of the seizure, usually in from ten to twelve. On the other hand, the gradual cessation of vomiting and purging, the reappearance of the pulse at the wrist, and the return of some warmth to the surface may herald convalescence. In such a case, after many hours' absence, the secretion of urine returns, and in a few days the patient may be practically well again. Usually, however, a condition, known as the "stage of reaction," gradually supervenes on the algide stage.

Reaction; cholera typhoid.—When the patient enters on this stage the surface of the body becomes warmer, the pulse returns, the face fills out, restlessness disappears, urine may be secreted, and the motions diminish in number and amount, becoming bilious at the same time. Coincidently with the subsidence of the more urgent symptoms of the algide stage and this general improvement in the

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appearance of the patient, a febrile condition of greater or less severity may develop. Minor degrees of this reaction generally subside in a few hours; but in more severe cases the febrile state becomes aggravated, and a condition in many respects closely resembling typhoid fever, "cholera typhoid," ensues. This febrile or possibly typhoid state may last from four or five days to perhaps a fortnight or even longer. In severe cases the face is flushed, the tongue brown and dry, and there may be delirium of a low typhoid character with tremor and subsultus; or the patient may sink into a peculiar torpid condition. The motions are now either greenish or like pea-soup, and may contain a larger or smaller amount of blood; at the same time they are very offensive. The reappearance of urine may be delayed from two to six days; at first scanty, high-coloured, cloudy, albuminous, and containing casts, it gradually becomes more profuse, paler and with less albumin. Though at first the urine is very deficient in urea, in uric acid, and in salts, later the quantity of these substances may exceed for a time the normal.

During the stage of reaction death may occur from a variety of complications; from pneumonia, from enteritis and diarrhœa, from asthenia, or from such effects of uræmic poisoning as coma and convulsions.

In cholera there is a considerable variety in the character of the symptoms and in their severity, both as regards individual cases and as regards different epidemics. It is generally stated that during an epidemic the earlier cases are the more severe, those occurring towards the end of the epidemic being on the whole milder.

Ambulatory cases occur during all epidemics. Such cases are characterised by diarrhœa and malaise merely; there is never complete suppression of urine, the diarrhœa never loses its bilious character, and it is not accompanied by cramps. The attack gradually subsides without developing a subsequent stage of reaction.

Cholerine.—In another set of cases the diarrhœa may be somewhat more acute, and the stools assume

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the well-known rice-water appearance; but the looseness soon ceases without leading to suppression of urine, or to algide symptoms, or even to very severe cramps, and without being followed by a stage of reaction. Such cases are sometimes designated "choleraic diarrhœa" or "cholerine."

Cholera sicca.—A very fatal type is that known as "cholera sicca." In these cases, though there is no, or very little diarrhœa or vomiting, collapse sets in so rapidly that the patient is quickly overpowered as by an overwhelming dose of some poison, and dies in a few hours without purging or any attempt at reaction. At the *post-mortem* examination the rice-water material, so characteristic of cholera, though it may not have been voided during life, is found in abundance in the bowel. Other cases die suddenly from apnœa caused, apparently, either by coagula in the right heart, or by spasm of the pulmonary arterioles, the lungs refusing to transmit the thickened blood. In certain cases, after temporary improvement, relapse may occur and is nearly always fatal.

Hyperpyrexia is an occasional though rare occurrence in cholera. In such the axillary temperature may rise to 107° F., the rectal temperature perhaps to 109° F. These cases also are almost invariably fatal.

Sequelæ.—Cholera is apt to be followed by a variety of more or less important sequelæ, such as anæmia, mental and physical debility, insomnia, pyretic conditions, chronic enterocolitis, nephritis, different forms of pulmonary inflammation, parotitis apt to end in abscess, ulceration of the corneæ, bed sores, and gangrene of different parts of the body. Jaundice occurs at times, and is said to be of the gravest import. Pregnant women almost invariably miscarry, the fœtus showing evidences of cholera.

Morbid anatomy and pathology.—*Rigor mortis* occurs early and persists for a considerable time. Curious movements of the limbs may take place in consequence of *post-mortem* muscular contractions. On dissection the most characteristic pathological appearances in cholera are those connected with the circulation and with the intestinal tract.

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If death have occurred during the algide stage, the surface presents the shrunken and livid appearance already described. On opening the body all the tissues are found to be abnormally dry. The muscles are dark and firm; sometimes one or more of them are discovered to be ruptured—evidently from the violence of the cramps during life. The right side of the heart and systemic veins are full of dark, thick, and imperfectly coagulated blood, which tends to cling to the inner surface of the vessels. Fibrinous clots, extending into the vessels, may be found in the right heart. The lungs are usually anæmic, dry, and shrunken; occasionally they may be congested and œdematous. The pulmonary arteries are distended with blood, the pulmonary veins empty. The liver is generally loaded with blood; the gall bladder full of bile; the spleen small. Like all the other serous cavities, the peritoneum contains no fluid, its surface being dry and sticky. The outer surface of the bowel has generally a diffuse rosy red, occasionally an injected, appearance. On opening the bowel it is found to contain a larger or smaller amount of the characteristic rice-water material, occasionally blood. The mucous membrane of the stomach and intestine is generally pinkish from congestion, or there may be irregularly congested or arborescent patches of injection here and there throughout its extent. In addition, there may be seen smaller or larger points of ecchymosis in or under the mucous membrane. The changes in the alimentary canal are most marked at the lower end of the ileum, where Peyer's patches and the solitary glands may be seen to be congested and swollen. In some instances the bowel is pale throughout; in many the mucous membrane has a sodden, pulpy appearance from exfoliation of epithelium—possibly a *post-mortem* change; occasionally, especially towards the lower end of the ileum, a croupous exudation is met with. The mesenteric glands are congested. The superficial veins of the kidneys are full; the medullary portion is much congested, the cortical portion less so; the tubules are filled with granular matter; the epithelium is

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cloudy, granular, or fatty, and, at a later stage, may be shed. The bladder is empty and contracted. Nothing special is to be noted in the nervous system.

If death have occurred during the stage of reaction, the tissues are moist; the venous system is less congested; the lungs probably congested and œdematous, perhaps inflamed. Very probably there are evidences of extensive enteritis.

Microscopical examination of the contents of the bowel during the acute stage of the disease discovers, in most instances, the comma bacillus. Usually it is in great abundance; occasionally in what is almost a pure culture. Sections of the intestine show the bacillus lying on and between the epithelial cells of the villi and glands. In no other organ or tissue of the body is the bacterium to be found. Therefore, assuming that the comma bacillus is the cause of cholera, we must conclude that the clinical phenomena are not the result of a septicæmia; but that they arise either from a local irritation produced by the bacillus, or from some toxin which it generates in the bowel and which is absorbed; or from a combination of these factors.

That the cholera vibrio is a powerful irritant is shown by the effect produced locally by a hypodermic injection of a virulent culture. When so injected, not only does it give rise to local œdema, but, unless precautions are taken, it causes in certain animals necrosis of the tissues and ulceration at the seat of injection. It is conceivable, therefore, that when in the course of the naturally acquired disease the bacilli proliferate in the bowel, they or their products act as an irritant to the mucous membrane and so provoke the hypercatharsis, and the consequent dehydration of the tissues, which are the dominating features of the disease. On the other hand, the hypodermic injection of cholera vibrio cultures is followed by smart febrile movement lasting from one to three days, evidencing the presence of a febrogenic toxin capable of producing constitutional symptoms. This fact, together with the rapid and intense prostration which, in

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some instances of natural cholera, appears to be out of all proportion to the amount of catharsis present, suggests that the lethal effects of the vibrio are attributable, not alone to the drain of fluid from the blood and tissues, but also to the absorption of a cholera toxin from the intestine. It is somewhat strange, however, if this toxin be anything more than a subsidiary element in the production of the symptoms in most instances of the naturally acquired disease, that catharsis is not one of the effects of the hypodermic introduction of the vibrio, and that fever is not an earlier and more prominent symptom in natural cholera. The modern tendency is to regard the clinical phenomena as the result partly of local irritation and partly of toxæmia; variation in the proportional intensities of the different clinical elements depending on the degree of virulence of the particular strain of microbe introduced, and on the circumstances and idiosyncrasy of the patient.

Diagnosis.—During the height of an epidemic the diagnosis of cholera is generally an easy matter; the profuse rice-water discharges, the collapse, the cold clammy skin, the cyanosis, the shrunken features, the shrivelled fingers and toes, the feeble, husky, hollow voice, the cold breath, the cramps and the suppression of urine, together with the high rate of mortality, are generally sufficiently distinctive. But in the first cases of some outbreak of diarrhœa, which may or may not turn out to be cholera, and the true nature of which for obvious reasons it is of importance to determine, correct diagnosis, though urgently required, may not be so easily attained.

Symptoms resembling true cholera may supervene in the course of an ordinary severe diarrhœa, and are very usual in cholera nostras, in mushroom poisoning, in ptomaine poisoning, in the early stages of trichinosis, and in a certain type of pernicious malarial fever. In none of these, however, is the mortality so high as in cholera. It may be laid down, therefore, that epidemic diarrhœa attended by a case mortality of over 50 per cent. is cholera.

In other forms of diarrhœa it is rare for the

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stools to be persistently so absolutely devoid of biliary colouring matter as they are in cholera. A careful inspection of the stools sometimes yields valuable information in other ways. Thus in mushroom poisoning, fragments of the mushrooms which caused the catharsis may be seen; in trichinosis, the microscope may detect the adult trichina. In choleraic malarial attacks the presence of the malaria parasite in the blood, the periodicity of the symptoms, their amenability to quinine, together with the character of the prevailing epidemic, generally combine to guide to a correct diagnosis.

The detection of the comma bacillus in the stools is now regarded as a positive indication of cholera. It would be rash, however, to affirm that a negative result from bacteriological examination of a single case is conclusive against its being cholera. Moreover, such examinations to be trustworthy have to be made by a skilled bacteriologist. According to Kanthack and Stephens, the following were the methods of bacteriological diagnosis practised by Klein during the threatened epidemic in 1893:—

"*Method* 1.—A flake from the dejecta is placed in peptone broth and incubated at 37° C. In twenty-four hours an abundant crop of vibrios is found in the superficial layers of the broth. This pellicle consists of a practically pure culture, or, at any rate, is a culture which easily allows of pure subcultures being obtained.

"*Method* 2.—A flake is placed in sterile salt solution or broth; it is shaken up, and from this gelatine or agar tubes are inoculated, and plates are made. In agar plates incubated at 37° C. numerous colonies may be found in twenty to thirty hours. In the gelatine plates, after two to three days' incubation at 20° to 22° C., numerous typical colonies can be got.

"*Method* 3.—A flake is placed directly into Dunham's peptone salt solution (1 per cent. peptone, 0·5 per cent. sodium chloride), or the Dunham's solution is inoculated after previous dilution of the material. The peptone solution, after six, eight, to ten hours' incubation at 37° C., shows a definite turbidity, due to the rapid growth of the comma bacilli; and the cholera-red reaction may be obtained. For speedy diagnosis this method is most valuable; in six to twelve hours, or, at latest, in sixteen hours, comma bacilli can be found in the superficial layers of the peptone solution, so that in twenty-four hours pure cultures and the cholera-red reaction can be obtained

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in secondary peptone tubes. Also, a positive result may be obtained by this method in cases in which the microscopical examination has failed to give definite evidence of the presence of vibrios."

The first two methods are applicable to those instances in which microscopical examination of the stools shows crowds of comma bacilli. Method 3 is specially applicable to those stools in which comma bacilli are in very small numbers.

Mortality.—The average case mortality in cholera amounts to about 50 per cent. Some epidemics are more deadly than others. As already mentioned, the mortality is greater at the earlier than at the later stages of an epidemic. To the old, the very young, the pregnant, the subjects of grave organic disease—particularly of the liver, kidneys, and heart—the dissipated, the under-fed, and the feeble, the danger is very great.

Quarantine prevention.—Theoretically, quarantine should be an efficient protection against the introduction of cholera into a community; practically, it has proved a failure. Unless they are stringent and thoroughly carried out, quarantine regulations can be of little use. Unfortunately, the temptation to evade such regulations is in proportion to their stringency. It is impossible to secure the absolute honesty and efficiency of every individual in a large body of men charged with the details of any system entailing great personal inconvenience and loss to travellers and merchants. Therefore, if the strength of the quarantine chain is to be measured by its weakest link, the chain must be weak indeed, as a very slight knowledge of human nature will lead us to suspect, and a very slight acquaintance with the working of quarantine as ordinarily practised will attest. Even if the utmost care, intelligence, and honesty succeed in excluding individuals actually suffering from cholera, or likely within a reasonable time to suffer from cholera, there is yet no guarantee that the germ of the disease may not be introduced. Koch and others have shown that sometimes the dejecta even of individuals apparently in good health and who have not suffered,

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or who may not subsequently suffer from choleraic disease, may yet contain, and for some time continue to contain the cholera vibrio. If the cholera vibrio be the germ of cholera, then such healthy, vibrio-bearing individuals may well suffice to start an epidemic. It is impossible, short of absolute and complete isolation, for any practicable system of quarantine to deal efficiently with such cases.

So far from ordinary quarantine proving a defence against cholera, it may actually increase the risk of an epidemic. This it does by fostering a false sense of security, and so leading to neglect of those well-proved guarantors of the public health—domestic, municipal, and personal cleanliness, and a pure water and food supply.

The system to which Great Britain apparently owed her immunity during recent epidemics on the continent of Europe is a practicable and, in civilised conditions, an efficient one. Under this system only ships which were carrying, or which had recently carried cholera patients were detained; and even these merely till they could be thoroughly disinfected. Thus inconvenience and loss to travellers and merchants were small, and the temptation to conceal cases of the disease or to evade regulations was proportionately minimised. Any cholera cases were isolated in suitable hospitals, the rest of the crew and passengers, although supervised for a time, being given free pratique. At the same time, attention was not diverted from the sanitation of towns, especially of seaports; this was the measure mainly relied on. Suspicious cases occurring on shore were at once reported to the sanitary authorities and promptly dealt with, fomites being destroyed or disinfected at as little cost and inconvenience to individuals as possible. Every endeavour was made to prevent fæcal contamination of the public water supply.

Of late years in India effort is being directed much on the same lines, attention being given to sanitation rather than to quarantine. During the great religious festivals the sanitary condition of the devotees is looked after so far as practicable, special

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care being given to provide them with good drinking and bathing water. Many of the large Indian towns now enjoy an abundant and pure water supply; and civilised systems of night soil conservancy and other important sanitary measures are being gradually introduced, in the case of more than one great city, with the most gratifying results.

Among the troops in India, on the appearance of cholera in their neighbourhood, special protective measures are promptly instituted, elaborate directions having been drawn up for the guidance of medical officers. For an account of these regulations the reader is referred to the Annual Report of the Sanitary Commissioner with the Government of India for 1895, Appendix, p. 189.

Incubation period.—All quarantine and protective systems must take cognisance of the fact that, although cholera may declare itself within a few hours of exposure to infection, it may also do so at any time up to ten days thereafter. Three to six days may be set down as the usual duration of the incubation period.

Anti-choleraic inoculations. — In 1885, during an epidemic of cholera in Spain, Ferran instituted a system of prophylactic inoculation. He injected hypodermically ordinary laboratory cultures of the cholera vibrio obtained directly from cholera corpses. No attempt was made to regulate or standardise in any way the virulence of the cultures. The results were not encouraging. As accidents were frequent, the Government put a stop to the practice.

In 1893 Haffkine, after elaborate experiments on the lower animals, commenced a system of anti-cholera vaccinations, using a pure virus of a fixed and known strength. This virus he prepared by passing the cholera vibrio through a series of guinea-pigs by means of intraperitoneal injections. In this way the microbes were increased in toxicity to a definite point beyond which their virulence could not be exalted. Cultures so prepared gave rise, when injected hypodermically, not only to a general but also to a local reaction, the latter being so severe

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that it ordinarily ended in extensive sloughing and ulceration. To avoid this undesirable result, a milder vaccine was prepared by cultivating the strong vaccine in artificial media at a temperature of 39° C., and in an atmosphere kept constantly renewed. By first injecting under the skin of animals this milder vaccine, it was found that such a measure of protection was conferred that subsequent injection of the strong virus was no longer followed by violent local reaction. Having satisfied himself that the subcutaneous injection of these two vaccines conferred immunity against the cholera vibrio in the lower animals, Haffkine proceeded to use them in man on a large scale in India, with the approval and aid of the Government. Up to 1895 70,000 injections of living cholera bacilli had been made in 43,179 individuals. In no instance did any bad result ensue. While admitting that the value of his method has not been fully proved, Haffkine claims that the results are sufficiently encouraging to justify a continuation of these inoculations on a larger scale.

The symptoms which these injections produce are fever, transient œdema and tenderness at the seat of injection, the first evidence of constitutional disturbance appearing from two to three hours after the injection is made. The fever and general indisposition last from twenty-four to thirty-six hours, the local symptoms gradually disappearing in from three to four days. The symptoms following the second injection—made from three to four days after the first—are generally more marked, but of shorter duration. The microbes injected die. It is the substances set free on their death which confer the immunity; for it is found that carbolised cultures—that is, dead vibrios—produce the same immunising and constitutional effects, though in a somewhat milder and probably less permanent degree. How long the immunity conferred by these injections endures has not been definitely settled. For details of Haffkine's original methods and technique see the *British Medical Journal*, Feb. 4, 1893, and the *Indian Medical Gazette*, Nov., 1896.

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In consequence of an experiment on himself, Haffkine found that, although the virulent comma bacillus produced necrotic effects at the site of inoculation in guinea-pigs, it did not do so in man. Accordingly, he has abandoned his original method of a primary inoculation with an attenuated virus, and has since countenanced immediate inoculation with virulent, recently-isolated vibrios, without further preparation. According to Powell, the method is as follows:—

"The whole surface of agar in a sloped tube is inoculated with the comma and cultivated for from twenty-four to thirty-six hours at a temperature of 40° C. The whole surface should then be covered with a uniform layer of growth. Sterilised water is then added to one-third the height of the agar, and the growth washed off and suspended in the water by rapidly rotating or shaking, till the surface of the agar is quite clear. Half a cubic centimetre, about nine minims, is the dose for an average adult."

Powell's results are highly favourable—namely, 198 cases of cholera with 124 deaths among 6,549 non-inoculated tea-garden coolies in Assam, against 27 cases and 14 deaths among 5,778 inoculated coolies. Had the incidence of cholera been the same in both classes, the inoculated would have had 174 instead of 27 cases, and 109 instead of 14 deaths.

Personal prophylaxis.—During cholera epidemics great care should be exercised to preserve the general health; at the same time, anything like panic or apprehension must be sedulously discouraged. Fatigue, chill, excess—particularly dietetic or alcoholic excess—are to be carefully avoided. Visits to cholera districts should be postponed if possible, seeing that the new-comer is specially liable to contract the disease. Unripe fruit, over-ripe fruit, shell-fish, food in a state of decomposition, and everything tending to upset the digestive organs and to cause intestinal catarrh are dangerous. Melons, cucumbers, and the like deserve the evil reputation they have acquired. Purgatives—particularly saline purgatives—unless very specially indicated, should never be taken at these times. All drinking water, and all water in which dishes and everything used

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in the preparation and serving of food are washed, should be boiled. Filters — except perhaps the Pasteur-Chamberland filter—are not for the most part to be relied on; in many instances they are more likely to contaminate the water passed through them than to purify it. A good plan in a household, or in public institutions, is to provide for drinking purposes an abundant supply of weak tea or lemon decoction, the supply being renewed daily; such a plan ensures that the water used in the preparation of the drink has been boiled.

Diarrhœa occurring during cholera epidemics should be promptly and vigorously treated.

Treatment.—During cholera epidemics it is customary to establish depôts where sedative and astringent remedies are dispensed gratuitously for the treatment of diarrhœa. Experience seems to encourage the belief that by such means incipient cholera may be aborted during the stage of premonitory diarrhœa. Of the various drugs used with this view, chlorodyne, or chlorodyne and brandy, is the most popular. Lead and opium pill; chalk, catechu and opium mixture; compound kino powder; aromatic powder of chalk and opium; a pill of opium, asafœtida and black pepper; dilute sulphuric acid and laudanum, are among the drugs more commonly employed for this purpose. Whether true cholera can be cut short in this way or not, it is certainly in the highest degree advisable at such a time to neglect no case of diarrhœa, but to insist on rest, warmth, and the greatest prudence in feeding in all cases of intestinal catarrh or irritation.

Many plans of treatment, based on theoretical considerations, have been advocated from time to time; so far, however, none of them has proved of material service in true cholera. The eliminative treatment advocated by Dr. George Johnson; the spinal ice-bag recommended by Chapman; various antiseptic methods directed to the destruction of the vibrio in the intestinal canal; drugs designed to counteract the physiological effects of the cholera toxins, as chloroform, atropine, nitrite of amyl, and

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nitro-glycerine, may be mentioned as belonging to this category of remedies.

Practically, the only treatment of any proved value in cholera is the purely symptomatic and expectant one. If our efforts have failed to counteract the premonitory diarrhœa, attention should be given to maintaining the patient in as favourable a condition as possible to struggle against the poison of the disease. He should be kept strictly in the horizontal position, in a warm bed, and in a well-ventilated but not too cold room. His thirst should be treated by sips of iced water or of soda-water, or champagne, or brandy and water. Copious draughts, as they are likely to provoke vomiting, are usually condemned. It does not follow from this that they are harmful; the emesis contributes to the elimination of germ and toxin. Cramps may be relieved by gentle frictions with the hand or with ginger-root, by a small hypodermic injection of morphia, or, these failing, by short chloroform inhalations. The surface of the body should be kept dry by wiping it with warm dry cloths, and the surface heat maintained by hot-water bottles or warmed bricks placed about the feet, legs, and flanks. The patient must not be allowed to get up to pass his stools; a warmed bed-pan should be provided for this purpose. All food should be withheld while the disease is active.

If the pulse fail or disappear at the wrist, stimulants by the mouth, or, if there is much vomiting and these do not appear to be absorbed, hypodermic injections of ether or brandy may be given. No improvement ensuing, intravenous or subcutaneous injection of normal saline fluid may be had recourse to. A suitable injection may be quickly prepared of common salt sixty grains, carbonate of soda sixty grains, boiled water one quart. Of this, from one to three quarts at a temperature of 100° F. may be slowly introduced by gravitation into a vein, the effect being carefully watched. The pulse can generally be quickly restored temporarily by this means and life prolonged, possibly in a few instances saved; too often, however, the fluid so introduced

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rapidly escapes by the bowel, and collapse once more sets in. Dr. Cox, of Shanghai, has had some encouraging results from continuous, prolonged, slow, intravenous injection of saline fluid, the fluid gravitating from a vessel placed two and a half feet above the level of the patient's arm. The flow is kept up for several hours, and as long as it is deemed that there is any risk of collapse.

During the stage of reaction, should purging persist, large doses of salicylate of bismuth with a little opium may prove of service. In these circumstances massive rectal injections of tannin one ounce, gum arabic one ounce, warm water one quart, are of use. If the secretion of urine is not quickly restored, large hot poultices over the loins, dry cupping of the same region, and the judicious use of bland diluents should be had recourse to. Stimulating diuretics are dangerous. Retention of urine must be inquired about, and the region of the bladder frequently examined, and, if necessary, the catheter employed. In the event of constipation, purgatives must be eschewed and simple enemata alone used.

In cholera convalescents the diet for a time must be of the simplest and most digestible nature—diluted milk, barley-water or rice-water, thin broths, meat juice and so forth—the return to ordinary food being effected with the greatest circumspection.

Cholera typhoid must be treated much as ordinary enteric fever.

Precautions.—It must never be forgotten by those responsible for the management of cholera cases that through their discharges such patients are a danger to the community, and that those discharges may contain the vibrio in some instances up to fifty days after the attack. Further, that though the germ dies in a few hours if dried, it preserves its vitality for many days if kept moist, as, for example, in damp, soiled linen; that it may live for months as a saprophyte in water or damp soil; and that it is not killed by ordinary cold. Therefore, all discharges and soiled linen from cholera cases should be

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immediately disinfected or destroyed, and every precaution must be taken during convalescence, as well as during the acute stage, to prevent contamination of wells, public water supply, drinking and table vessels, and food. The domestic fly and other vermin as vectors of the germ must not be overlooked.

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CHAPTER XXVII

DYSENTERY

Definition.—A term applied to a group of diseases of which the principal pathological feature is inflammation of the mucous membrane of the colon, and of which the leading symptoms are pain in the abdomen, tenesmus, and the passage of frequent small stools containing slime, or slime and blood.

Geographical distribution.—From time to time forms of dysentery have extended as epidemics of great severity over vast tracts of country. These great epidemics, or, rather, such of them as have been recorded, have been confined principally to temperate latitudes. There can be little doubt that similar visitations have occurred and do occur in tropical countries. At the present day dysenteric disease is rare in Britain. Small circumscribed epidemics break out occasionally among the general population, and in certain public institutions, particularly lunatic asylums, endemic dysentery is common; but, in comparison to what was the case in pre-sanitary days, and with what obtains in tropical countries at present, our indigenous dysentery is altogether insignificant. The same remark applies to the continent of Europe. But when, in Europe or elsewhere, war breaks out, or when there is widespread scarcity of food, dysentery is almost sure to appear. In most places in the tropics dysentery of one form or another is always to be found; in some places and seasons more than in others. On the whole, it may be advanced that wherever the general hygienic conditions are bad, wherever the soil is much fouled by excreta, especially where the water supply is polluted, wherever many people are crowded together in one building or camp, where the food is coarse, monotonous or unsound, there, especially in tropical and

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sub-tropical climates, dysentery is or becomes endemic, and may become epidemic.

Amongst tropical diseases the group of morbid conditions included by the general term "dysentery" ranks in importance next to malaria. Unfortunately, our knowledge is not in proportion to the importance of the subject. Until recent years the word "dysentery" was supposed to indicate a single well-defined disease; writers described its ætiology, symptoms, pathology, morbid anatomy, and treatment with precision. Lately we have begun to get beyond this stage of confident ignorance. We may know something about the symptoms and morbid anatomy of dysenteric disease, but we are obliged to confess that we know very little about the real cause of the malady. We cannot even say for certain whether there is but one disease having grades of severity, or a dozen specifically distinct diseases included under the term dysentery. This knowledge of our ignorance, although promising well for future advance, is for the present extremely embarrassing to the student, and more especially to the writers of text-books. Anything approaching a scientific description is as yet impossible. I am compelled, therefore, in describing dysentery, to adopt an arbitrary, unscientific, and purely clinical classification; and to deal with effects before discussing possible causes, symptoms before ætiology.

Symptoms.—In ordinary cases the leading symptoms of dysentery are those of inflammation of the great intestine—namely, griping, tenesmus, and the passage of frequent, loose, scanty, muco-sanguineous stools. The illness commences in various ways—insidiously or suddenly; with high fever, with moderate fever, or without material rise of temperature. Or the symptoms of colitis may be grafted, as it were, on to some general affection such as scurvy, or malaria, or on to some chronic disease of the alimentary canal, such as sprue. They may assume acute characters; or from the outset the symptoms may be subdued and of little urgency. As a rule, the symptoms are proportioned to the extent of the disease, but they

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are not necessarily so. In certain cases they may be extremely urgent and in apparent disproportion to the area of bowel affected; or they may be, in comparison to the extent and the degree of the anatomical lesion, disproportionately trifling; or they may be altogether absent, even when the colon is extensively diseased. There is, therefore, endless variety in their character, urgency, and significance. As a general rule, the nearer to the rectum the lesions, the more urgent the tenesmus; the nearer to the cæcum, the more urgent the griping. These two symptoms, together with the presence of points of localised tenderness, form, in many cases, a fair guide to the location and extent of the lesions.

Clinically, the dysenteries are conveniently arranged according to what may be presumed to be the gross characters of the attendant intestinal lesion.

Catarrhal dysentery.—A common history to receive is that for some days the patient had suffered from what was supposed to be an attack of diarrhœa. The stools, at first copious, bilious, and watery—perhaps to the number of four or five in the twenty-four hours—had latterly, and by degrees, become less copious and more frequent, less fæculent and more mucoid, their passage being attended by a certain and increasing amount of straining and griping. On looking at what was passed, the patient had discovered that now there was very little in the pot except mucus tinged, or streaked, or dotted with blood; a tablespoonful, or thereabouts, being passed at a time. By degrees the dysenteric element entirely supplanted the diarrhœa; so that when seen by the physician the desire to go to stool had become almost incessant, the effort to pass something being accompanied by perhaps agonising griping and tenesmus. The patient has hardly left the stool before he has a call to return to it, and he may be groaning and sweating with pain and effort. The suffering is sometimes very great; nevertheless, with all this suffering there is often very little fever, the thermometer showing a rise of only one or two degrees.

In another type of case the incidence of the

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dysenteric condition is much more abrupt. Within a few hours of its commencement the disease may be in full swing. The stools, at first fæculent, soon come to consist of little save a yellowish, greenish, or dirty brown mucus—blood-tinged or streaked and dotted with little hæmorrhages. Very soon the desire to stool becomes increased, the griping and tenesmus being accompanied, perhaps, with most distressing dysuria. The patient is glued, as it were, to the commode. Fever, which at the outset may have been smart and preceded by rigor, subsides, so that when the patient is seen it may be absent or inconsiderable. The tongue soon becomes white or yellow-coated; there may also be thirst; very generally anorexia is complete.

In either case, after perhaps four, five, or six days, the urgency of the symptoms may gradually diminish and the acute stage taper off into a subacute or chronic condition; or it may terminate more quickly in perfect recovery.

Ulcerative dysentery.—Should, on the contrary, the disease advance, the urgency of the symptoms shows hardly any abatement; the stools become very offensive, and now contain, besides blood, large or small shreddy, ash-coloured, stinking sloughs. This may go on, better or worse, for days or weeks. Recovery from this condition is, necessarily, a slow process, seeing, as the presence of sloughs in the stools indicates, that there is deep ulceration which must take some time to cicatrise. Such a condition tends to drift into that most dangerous and most distressing complaint, chronic dysentery, relapsing and improving during many months or even years, and causing, if severe and prolonged, great wasting, pain, and misery.

Fulminating dysentery.—The attack generally begins suddenly, often in the middle of the night, with chills or smart rigor, vomiting, headache, and a rapid rise in temperature to 102° to 104°F. Coincident with the rigor, or very soon afterwards, but occasionally not for a day or two, purging begins, the stools quickly assuming dysenteric characters. In from two or three days to a week or thereabouts, fever persist-

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ing to the end, or collapse setting in with a subnormal temperature, the patient dies. So virulent is the blood poisoning in some instances that death may take place before dysenteric stools are emitted, and it is only the presence of an epidemic of dysentery at the time, or the *post-mortem* revelations, that make diagnosis possible. The mortality in such cases is very high. Occasionally the acute phase subsides, the patient slowly recovering after passing through the ulcerative phase of the disease.

Relapsing dysentery.—In a proportion of dysenterics, although the activity of the initial attack may subside somewhat, symptoms do not completely disappear. The stools may recover their fæculent character and even show some formation, but they continue to be passed too frequently, are often preceded by griping, and contain a variable amount of slime and muco-pus, with or without blood. Without obvious cause, or as a sequel of some dietetic or other indiscretion, these dysenteric signs become aggravated, and there is once more a recurrence of active symptoms. Spontaneously, or through treatment, matters quiet down again, presently however to be followed by another relapse; and so on, until after weeks or months of suffering the patient dies of exhaustion or slowly recovers. This is the type of dysentery, as shall be explained presently, that some authors claim to be produced by *amœbæ*, and designate "amœbic dysentery."

Recurring dysentery.—The patient has an attack of dysentery from which recovery appears to be complete. Months, or even years subsequently, without recognisable fresh exposure to infection, and during prolonged residence perhaps in a non-endemic district or country, the disease recurs, to subside and recur at intervals for several years. I have several times seen such cases. They can only be explained by assuming a remarkable capacity for prolonged latency on the part of the special dysenteric virus concerned.

Chronic dysentery.—In a large proportion of cases of acute dysentery the bowel does not become absolutely healthy for a considerable time after

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abatement of the more urgent symptoms. On the slightest dietetic imprudence, after chill or fatigue, or even slight indulgence in alcohol, the old symptoms reappear. In such cases sudden attacks of diarrhœa are common. Some patients for months, or even years, never pass a perfectly healthy stool, the unformed motion always containing slime or mucopus, and at times blood. Often there is a tendency to scybalous stools, or to constipation alternating with diarrhœa. If such symptoms are at all severe, or persist for a long time, the digestion may deteriorate, and the patient become thin and cachectic, his complaint assuming many of the characters of sprue. On the other hand, general nutrition may not suffer, although the patient may continue for years to pass two or three unhealthy stools daily. In mildness and severity, the more chronic types of dysentery are as manifold and varied as are the earlier and more acute phases of the disease.

Anomalous types of dysentery have been described from time to time. Thus in a special report on an outbreak among Polynesian immigrants to Fiji which occurred on board ship in 1890, Daniels describes a disease of high fatality (fifteen deaths in thirty-one cases), manifestly infectious, running a rapid course—death taking place in from two to ten days. In six cases there was extensive superficial ulceration of the mouth, and in two cases diphtheritic inflammation of the prepuce. *Post-mortem* examinations were made in four cases. In all, the whole of the colon and at least half of the small intestine were found acutely inflamed, superficially ulcerated, or covered with a firm, dry, green or grey layer adherent to or continuous with the subjacent intestinal wall. In a special report (1898) Dr. Corney, of Fiji, remarks that at least six similar epidemics had occurred in Melanesian immigrant vessels in twelve years. The high degree of infectiveness, the diphtheritic lesions in intestine and prepuce, and the great mortality clearly indicate a special form of enterocolitis.

Gangrenous dysentery.—What is known as gangrenous dysentery is, symptomatically, but

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an aggravated form of acute ulcerative dysentery, or a sequel of the fulminating type. Instead of being mucoid, the stools come to consist of a sort of a thin dirty fluid, like the washings of flesh. On standing they deposit a grumous, coffee-grounds-looking material, and they stink abominably. Now and again sloughs of every shape, size, and colour, from ash-grey to black, are expelled. Sometimes tube-like pieces, evidently rings of mucous membrane which have been cast off *en masse*, are discharged. In such cases the patient rapidly passes into a state of collapse. He sweats profusely; the features, the extremities, and even the whole body, are cold and pinched as in the algide stage of cholera; he may vomit from time to time, and the belly may become distressingly tympanitic. In this condition there is usually a persistent and worrying hiccough. Low muttering delirium sets in; the pulse becomes small and running, and the patient rapidly sinks. Recovery is extremely improbable. Nevertheless, such cases have recovered, and must not necessarily be despaired of.

Hæmorrhage.—Whenever in dysentery sloughs separate, smart hæmorrhage is always possible. Sudden collapse may occur from this cause, even in otherwise mild cases. As in typhoid, the occurrence of hæmorrhage is more or less of the nature of an accident, depending, as it does, on the position of the sloughing sore in relation to an artery; of course, the more extensive and the deeper the sloughing, the greater the liability to hæmorrhage.

Perforation.—Another grave, though fortunately rare, accident in the course of dysentery is the occurrence of perforation. Should this unhappily take place, and if the patient survive the shock of an extensive extravasation into the peritoneum, symptoms of peritonitis will supervene and rapidly prove fatal.

Intussusception.—Intussusception is also an occasional occurrence, especially in children. It is not always readily recognised. A sudden increase of pain, increased straining, entire absence of fæcal matter from

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the stools, vomiting, and perhaps the presence of a tumour in the rectum, might lead one to suspect and examine for this accident.

Tenderness; thickening.—The abdomen is tender in most cases of acute dysentery. If the disease be of some standing a certain amount of thickening may be felt along the track of the colon, particularly over the sigmoid flexure.

Hepatitis.—In acute cases the liver is usually distinctly enlarged, and may be tender. It sometimes happens that attacks of hepatitis seem to alternate with attacks of dysentery; or, rather, that hepatitis increasing, dysenteric symptoms decrease, and *vice versâ*. These are always very anxious cases, and too often eventuate in the formation of an abscess or multiple abscesses in the liver; in the latter event they almost necessarily prove fatal.

Sequelæ.—Apart from chronic intestinal troubles, dysentery may be followed, as is the case in so many other infections, by peripheral neuritis. A condition resembling gonorrhæal rheumatism has frequently been noted as a sequel, and at least one epidemic has been recorded in which a large proportion of the cases became affected in this way. Abscess of the liver is the most important of the sequelæ of dysentery; it will be treated of separately, and need not be further alluded to here.

Mortality.—Although every now and again cases are met with which prove directly fatal, being overwhelmed by the initial dose of virus, or from the shock of an extensive and intense lesion, or from rapid exhaustion from hæmorrhage, or from perforation; and though some epidemics exhibit a malignancy which, fortunately, is not very common, the direct and immediate mortality from this disease is, under modern methods of treatment, not very high. In India, the case mortality in dysentery among Europeans ranges from 3 to 22 per cent.; among natives, about 37 per cent. In Egypt, Griesinger stated it as 36 to 40 per cent. In Japan, Scheube places it at 7 per cent. These figures are of little value, as so much depends on the place, the type of the epidemic, and the range of cases

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covered by the statistics. There was a time when, under a spoliative treatment by bleeding and calomel, dysentery proved a very fatal disease indeed. Even now, in the presence of scorbutus, famine, the stress of war, and similar conditions, whenever dysentery becomes epidemic in a community it is apt to claim a large number of victims.

Sequelæ more dangerous than the disease.—As a rule, under modern treatment, it is the sequelæ of the disease that we have to fear rather than the disease itself. The chronic ulceration, the scarring, thickening and contractions of the gut are irremediable conditions which too often, after months or years of suffering, lead to intestinal obstruction or, very frequently, to atrophy of the glandular and absorbent system of the entire alimentary tract, general wasting and fatal asthenia. Such patients hardly ever pass a healthy motion; they are troubled with chronic indigestion; at times they pass their food unaltered; they have recurring attacks of diarrhœa; they are flatulent; their tongues are red, often ulcerated and tender; they develop the condition known as "sprue," and sooner or later almost invariably succumb.

Morbid anatomy and pathology.—We were able to study the cognate subject of malaria scientifically; we could point out its germ or cause and, in a measure, indicate the way in which this germ produced pathological effects. Unfortunately, in the case of dysentery this cannot be done. Although in many instances the specific nature of the disease is not to be doubted, the specific body or germ has not in every type of the disease been indicated with anything like certainty.

The term dysentery includes, probably, several diseases.—As already hinted, there is good reason to believe that the term "dysentery" includes not one but several distinct diseases. We know that the symptoms grouped under this word are apt to differ in intensity and character in different places and in different epidemics. Some forms of the disease run a more or less definite course, and then terminate for good. Other forms exhibit a remarkable disposition

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to relapse. The dysentery of certain tropical countries, as the East Indies, is prone to eventuate in abscess of the liver; that of temperate climates and certain tropical countries, as the West India islands (except as regards one or two of those epidemics of which we have trustworthy accounts), is seldom succeeded or accompanied by hepatic suppuration. Some dysenteries are remarkably amenable to ipecacuanha; others appear to be uninfluenced by this drug. These and other circumstances seem to point to radical differences in the several forms—differences of cause as well as differences of symptoms, course and sequelæ. It is well, therefore, in considering the subject from a pathological standpoint, to regard the term "dysentery" as but the name for a group of symptoms indicating an inflamed condition of the colon—much in the same way as we regard cough as symptomatic merely of lung disease, and not as indicating a single and well-defined disease. Dysentery simply means inflammation of the colon. There are many kinds of inflammation of the colon.

Morbid anatomy of catarrhal dysentery.—In those cases that subside in a few days, whether spontaneously or in consequence of treatment, it is reasonable to suppose that the pathological condition consists only, or mainly, in congestion or in catarrhal inflammation; that here and there, or throughout its extent, the mucosa and perhaps submucosa are slightly swollen and congested; and that the surface of the former is softened, perhaps eroded, and covered with a blood-streaked glairy mucus of the same character as that which appears in the stools.

Morbid anatomy of ulcerative and gangrenous dysentery.—Cases of catarrhal dysentery rarely die; the exact conditions of the mucous membrane, therefore, in these cases can only be conjectured. It is otherwise in the severer forms of the disease. When such cases come to the *post-mortem* table, the mucous membrane of the large intestine and, very frequently, a foot or two of the lower end of the ileum are found to be thickened, congested,

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inflamed, speckled perhaps with ecchymoses, œdematous, and more or less riddled with ulcers or patches of gangrene of various sizes, shapes, and depths. As a rule, the brunt of the disease falls on the sigmoid flexure and descending colon; not unfrequently, the lesions are equally, if not more advanced in the cæcum and ascending colon, and may involve a foot or two of the lower end of the ileum. On the whole, the transverse colon, though often seriously implicated, is so to a less extent than one or other of the parts mentioned, or than the hepatic and splenic flexures.

The dysenteric ulcer varies in size from a punched out-looking sore the size of a pea, or even less, to a patch several inches in diameter. As a rule, in the earlier days of the acute stage, the ulcers tend to follow the folds of the mucous membrane, the free borders of which are the parts most liable to implication. The edges of the sores are ragged and undermined, the floor is sloughy and grey. There may be considerable thickening of the edges and base of the ulcer, and there may be peritoneal adhesions. The appearance of the ulcer may suggest that it extends by a process of burrowing in the submucosa, the superjacent membrane sloughing or disintegrating in consequence of the destruction of its subjacent nutrient vessels. This burrowing may extend for a considerable distance beyond the apparent margin of ulceration; so much so that long, suppurating, fistulous tunnels may connect one ulcer with another. In this way large patches of mucous membrane come to be undermined, and subsequently to slough away. Sores so formed are necessarily ragged and irregular in outline, and may even surround pieces of comparatively healthy mucous membrane. The floor of the active dysenteric ulcer may be, and generally is, formed of a sloughy material lying on the muscular coat; but the sore may penetrate deeper than this, and include the muscular coat itself, and even the serous membrane. The largest ulcers are generally found in the sigmoid flexure and descending colon; they are also frequently, though more rarely, found in the cæcum, the magnitude of

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the lesions diminishing as we trace the bowel upwards or downwards, as the case may be.

Along with the ulceration there is intense congestion of the non-ulcerated parts of the mucous membrane. In places there may be œdema of the submucosa; there may be small abscesses which elevate the mucous membrane; and there may also be distension of the solitary follicles by a mucoid or purulent material. In some instances a large portion of the mucous membrane may be seen to have died *en masse* and become gangrenous. In such, extensive sloughs may be thrown off as a sort of tube, apt to be mistaken during the lifetime of the patient for a diphtheritic cast of the bowel.

Morbid anatomy of fulminating dysentery.—Strong and Musgrave thus describe the lesions in this type of dysentery as it occurs in the Philippine Islands:—"In the most acute cases (death after three or four days' illness) the mucous membrane of the large intestine presents in general a reddened, swollen, puffy appearance. There is a superficial necrotic mucous layer which generally extends over the mucosa throughout the large bowel, and sometimes for a distance of 10 or 12 cm. into the ileum. This necrotic layer consists of mucus, red blood corpuscles, leucocytes, epithelial cells, many large swollen granular cells, and bacteria. No amœbæ are found. If one brushes the mucous layer lightly aside with the finger the bright-red injected appearance of the intestinal wall becomes more plainly visible. Dotted here and there throughout are small, diffuse, bright-red hæmorrhages with irregular margins measuring from 2 to 4 mm. in diameter, or even more. The solitary follicles are generally swollen and raised, and of a bright-red colour. Here and there, scattered among them, bright-red, sharply circumscribed, small purpuric spots may appear. Occasionally the background of the intestine may be described as though covered with a bright-red eruption, but with darker red hæmorrhagic points scattered over this background. In the acute cases no definite ulceration takes place, but only a superficial coagulation necrosis of the mu-

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cosa." The lower end of the ileum may be similarly affected. Mott's description of the lesions in the fulminating form of asylum dysentery, as it occurs in England, agrees practically with the foregoing. He adds: "Acute fatal cases of a little longer duration show the same swelling, but now frequently the mucous lining, although swollen, presents a pale grey or dirty whitish-grey appearance; the surface is sometimes finely or coarsely granular. This is owing to stasis in the vessels of the sub-mucosa and necrosis of the epithelium, and the formation of a *false membrane*, consisting for the most part of leucocytes and disintegrating epithelial cells."

The primary lesion.—Such, briefly, are descriptions of the principal lesions found in the acute stage of fatal dysenteries. There is general agreement among pathologists about these; but there is very great discrepancy of opinion as to the exact nature of the primary and essential lesions. Some maintain that the starting-point of the disease is in the solitary follicles, which, becoming distended by a specific exudation, afterwards slough, and form the starting-point for a spreading ulcer. Other pathologists regard the primary lesion as being altogether independent of the glandular structures of the mucous membrane. They hold that, in consequence of the irritation produced by the specific cause of dysentery, an exudation is thrown out on to and into the mucous membrane itself: a slough is formed of this, the implicated piece of tissue being subsequently got rid of, very much in the same way as the slough forming the core of an ordinary boil. Another primary lesion described is the small abscess, alluded to as elevating the mucous membrane and projecting into the lumen of the gut. These minute, pimple-like abscesses consist of a collection of gummy pus. After a time a tiny opening forms at the apex of the little swellings, through which the contents may be expressed: it is this opening which, it is alleged, forms, on enlarging, the specific ulcer of dysentery.

Assuming that there are several specific causes for

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dysentery, it is to be expected that the corresponding primary lesions should differ; that whilst one causes a suppurating or a gangrenous lesion, another may produce a croupous or a diphtheritic; that whilst one species of dysenteric germ attacks the mucosa, another species may select the sub-mucosa; one may attack the glandular structures, another the connective tissue, another the epithelial layer. Whatever the primary lesion may be, eventually the weakened tissues are attacked by the ordinary bacteria of suppuration; so that ultimately, if the cases survive long enough, they all present a certain uniformity as regards the ultimate ulceration, thickenings and other inflammatory lesions disclosed *post-mortem*.

Healing process.—The dysenteric ulcer heals partly by contraction, partly by the formation of a very thin scar tissue—scar tissue which, besides contracting, is apt to become pigmented. Lost glandular structures are never reproduced. Owing to the constant peristaltic movement of the gut, and the passage of fæces over the face of the healing ulcer, cicatrisation, as might be supposed, is a slow process, and one prone to interruption by recurring attacks of inflammation of a more or less specific nature.

Lesions in chronic dysentery.—In chronic dysentery the ulcers are usually smaller and less numerous than in the acute disease. They are also less ragged in outline, tending to become circular in shape and to acquire thickened rather than undermined edges. Cicatricial bands and contractions may narrow the lumen of the gut, the functions of which are still further hampered by thickenings, or by adhesions which unite and bind it to neighbouring organs. Dilatation above the seat of cicatricial stricture is liable to ensue. In chronic dysentery large patches of the bowel, and even the ulcers themselves, may be pale and anæmic, whilst at the same time other patches of the gut are congested. Some parts may be thickened and contracted; others, again, may be thinned and dilated, the glandular structures being atrophied.

Polypoid growth.—Some time ago I attended a case of chronic relapsing dysentery in which the

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mucous membrane—at all events of the rectum and descending colon—was covered with enormous numbers of polypoid growths of considerable magnitude, some of them at their free ends being as large as the tip of the little finger. The growths had pedicles one to two inches in length. During life these polypoid bodies appeared in the stools, often in great number, looking like so many mucilaginous seeds. Similar cases are occasionally met with.

Liver; mesenteric glands.—In by far the majority of cases of acute dysentery, the liver is hyperæmic and swollen. In about one-fifth of the cases of Indian dysentery which come to the *post-mortem* table, the liver is the seat of single or multiple abscesses. In chronic dysentery this organ may be atrophied; very generally it is the subject of fatty degeneration.

In acute cases the mesenteric glands are enlarged, soft and congested, or even hæmorrhagic; in chronic cases they are enlarged, hard and pale. None of the other viscera is characteristically affected. Abscess is sometimes discovered about the rectum. If perforation has occurred, there may be signs of commencing peritonitis.

Ætiology.—From a study of the natural history of the various types of the disease we are forced to the conclusion that at least three factors are concerned in the production of the clinical condition called dysentery, namely, (1) influences that weaken the natural resistance of the bowels, such as the depressing or congesting effects of chill, bad food, purgatives, intemperance, intestinal nematodes and trematodes. These prepare the ground for the action of (2) the specific germs which have their action supplemented subsequently by (3) the ordinary bacteria of suppuration and ulceration. It must be with the mucous membrane of the bowels in these respects as it is with the skin of the surface of the body. For example, a traumatic erythema leads to a specific eczema which, in turn, may end in an ulcer. So with the bowel: a debauch, a chill, or bad food may lead to an intestinal catarrh. A specific germ, which in healthy conditions would not have proved pathogenic, coming on the scene

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produces a lesion of the mucosa, in which the ubiquitous pus germs find their opportunity.

Three types of dysentery, correlated to three kinds of parasites, are now fairly well made out. These are not mutually exclusive; one type may be superposed on and complicate another. That there are other dysenteries, similarly correlated to parasites as yet unrecognised, is not to be doubted. The recognised types and their respective parasites are as follows:

1. BACTERIAL—
   Bacillary dysentery.
   Bacillus dysenteriæ (Shiga).
   Bacillus pyocyaneus.
   Durham's micrococcus (?).
2. PROTOZOAL—
   Amœbic dysentery.
   Amœbæ.
   Balantidium dysentery.
   Balantidium coli.
   Kala-azar dysentery.
   Leishman-Donovan body.
   Malarial dysentery.
   Malaria parasites.
3. VERMINOUS—
   Schistosomum japonicum.
   Schistosomum hæmatobium.
   Œsophagostomum brumpti.

In this place I shall discuss briefly (1) bacillary dysentery; (2) amœbic dysentery; (3) balantidium dysentery. Reference to the other forms will be found under their respective parasites.

BACILLARY OR EPIDEMIC DYSENTERY.

The characteristics of this type of dysentery, at all events of that type of bacillary dysentery which has received of late so much attention, are acuteness of onset, often a well-marked initial fever, when recovery has taken place little tendency to relapse, the presence of *Bacillus dysenteriæ* in the stools, an

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initial diptheroid necrosis of the mucosa of the large intestine, non-liability to abscess of the liver occurrence in epidemic form and in all latitudes.

Celli and Fiocca believed that dysentery is caused by *Bacterium coli commune*, which, they asserted, is always present in the stools in this disease. Generally non-pathogenic, this bacterium, they stated, acquires in certain circumstances virulent properties. They said that in the bowel it is often associated with a bacillus like that of typhoid, as well as with streptococci; and they asserted that introduced by the mouth, or injected by the rectum, any or all of these, particularly when in combination and in certain not understood circumstances, either singly or in combination, excite dysentery. They supposed that what they call *Bacterium coli dysenteriæ* is but a variety of *Bacterium coli commune*, a variety brought about in some way by the presence of the other bacteria mentioned; that in consequence of the presence of these other bacteria *Bacterium coli commune* acquires the power of secreting a specific toxin, which power it retains on being transferred from one human being to another. The toxin can be precipitated by alcohol from cultures, and has the property of giving rise to dysentery when administered by the mouth, the anus, or hypodermically.

Shiga was the first to call marked attention to what is now known as *Bacillus dysenteriæ*, which Celli now regards as identical with the organism just alluded to. Flexner, Strong, Musgrave and others regard it as the cause of what they termed *epidemic dysentery*, in contradistinction to *sporadic* or *endemic dysentery*, which they regard as belonging to the pathogenic sphere of *Amœba coli*. It is a bacillus with rounded ends, varying in size somewhat according to the culture medium, from 1 to 3 μ in length by ·4 to ·5 μ in breadth. It closely resembles in its properties *Bacillus typhosus*, but is less mobile, displaying a more uniform generation of indol; after a brief preliminary acid production in milk, it gives rise to a gradually increasing alkalinisation; it does

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not agglutinate in serum from typhoid cases, but reacts in serum from dysenteric cases to which *B. typhosus* does not respond (Flexner). It possesses lateral flagella when first recovered from the stools, but it loses these on repeated culture. It occurs in greatest abundance in dysenteric lesions and in the mucus in the stools during the most acute stage of "epidemic" dysentery. It is pathogenic to many animals, although it does not produce in them, or only exceptionally, dysenteric lesions. In two experiments on man, one intentional, the other accidental, ingestion of the pure cultures was followed, within a short time, by well-marked symptoms of dysentery. It agglutinates with the blood serum of "epidemic" dysentery in dilutions of 1 in 10 to 200. Furthermore, Shiga claims by immunising animals to have produced a serum which has reduced the mortality in "endemic" dysentery in Japan from about 35 per cent. to 9 per cent.

The cultural characters of *B. dysenteriæ* are subject to great variation. As a consequence considerable confusion has arisen, but it is more generally conceded that, though indicating different strains of bacilli, these differences are not specific. In this connection Blackham has published (*Lancet*, Dec. 1, 1902) the useful table which will be found on pages 438–439.

In the *Journal of Experimental Pathology* (1898) there appears an account of a limited but very fatal epidemic in the United States in which *Bacillus pyocyaneus* was found. Calmette and Maggiora report that they also have encountered this bacterium in dysentery, as well as in infantile diarrhœa.

Durham's micrococcus.—Durham has described an exceedingly minute micrococcus—so minute that it passes through a Berkefeld filter—which he separated from the blood, liver, spleen, kidney and bile in seven cases of asylum dysentery. The investigation is as yet incomplete, but there are some grounds for supposing that this micro-organism may turn out to be the germ of at least one variety of the very fatal

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type of dysentery, euphemistically termed "colitis," which is the scourge and disgrace of lunatic asylums. Assuming this to be the case, from the fact that the micrococcus occurs throughout the organs, the dysenteric lesion must be regarded as symptomatic of a general infection.

AMŒBIC DYSENTERY.

As distinguished from other forms the characteristics of this type of dysentery are generally insidious onset, marked tendency to chronicity, relapses alternating with periods of comparative quiescence, great liability to abscess of the liver, confinement to warm climates or the warm season of temperate climates, local endemicity, the presence of amœbæ in the stools and implicated tissues. The intestinal lesion consists primarily of small amœbic abscess formations in the submucosa and the subsequent undermining and necrosis of the superjacent mucosa.

As a practical point it may be mentioned that amœbic dysentery may concur with bacillary, or with balantidium, or with verminous dysentery. This circumstance must not be overlooked, either in practice or in pathological studies.

The Amœba.—The discovery of the presence of amœbæ in the stools of dysenterics, originally pointed out by Lösch, naturally created much interest. Although within the last few years a large literature has grown up around the subject, and although some definite conclusions both as regards the bionomics of the amœba and its relationship to the disease have been arrived at, much confusion and uncertainty still remain. Originally regarded by pathologists as a single and definite organism and called *Amœba coli*, it now appears that there are probably several distinct species of amœbæ to be found in the intestinal canal of man, some of which are pathogenic, others possibly harmless. Schaudinn maintained that there are two well-defined species; these he named respectively *Entamœba coli* and *Entamœba histolytica*. The former he regarded as non-pathogenic, the latter as the specific germ of amœbic dysentery. The

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TABLE SHOWING THE MORPHOLOGICAL AND CULTURAL CHARACTERISTICS OF BACILLUS DYSENTERIÆ AND THE ALLIED GROUP OF MICRO-ORGANISMS.*

MICRO-ORGANISM.	CHARACTER.	MOTILITY.	FLAGELLA.	GROWTH ON NUTRIENT AGAR.	GELATIN STAB.	PEPTONE AND SALT.	NEUTRAL RED SHAKE.	LITMUS MILK.	STERILE POTATO.	AGGLUTINATION WITH DYSENTERIC SERUM.
Shiga's bacillus dysenteriæ I.	Short rod with rounded ends. No spores. Length 1-3 μ.	Motile in recent cultures from stools. Gradually loses motility in sub-cultures.	2-6. Mostly terminal. Rather short and thick.	Semi-opaque. Resemble the growth of bacillus typhosus, but are more transparent.	Similar to bacillus typhosus, but film which spreads out from puncture usually absent.	Faint haziness which rapidly clears. No indol.	No appreciable discharge of colour.	Becomes feebly acid. After 4 days' incubation acidity has been estimated as equal to 6 per cent. decinormal alkaline solution. No clot.	Transparent or whitish growth, which becomes brownish red or dirty grey, with discoloration of potato at edge in a few days.	Usually only agglutinates with serum from animal immunised by special strain of bacillus dysenteriæ
Shiga's bacillus II.				Has a characteristic odour called by the Germans "Sperm-geruch."	Growth not seen till 48 hours and then only slight white growth.	"	"	"	"	"
Vaillard's bacillus.	Shorter than Shiga, otherwise similar.		Numerous fine, reticulated, very long and readily seen (Birt).		"	"	"	"	"	"
Flexner's bacillus.	Similar to Shiga.		Long, thick, and terminal.				"	"	"	"

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Kruse's bacillus.	"		Usually 2 terminal.				"	"	"	"
Pseudo-dysenteric bacillus.	Generally somewhat larger than true dysentery bacillus.		Variable.	"	"	"	"	Slightly acid at first. Afterwards slightly alkaline.	"	Very variable.
Bacillus typhosus abdominalis.	Longer than either bacillus dysenteriæ or bacillus coli. "Oval ends" (Muir and Ritchie).	Sub-cultures always very motile.	8-12.	More opaque than those of bacillus dysenteriæ.	Similar, but surface film usually present.	"	"	Slight acidity after some days.	For several days apparently no growth. Later slight pellicle with velvety surface.	*Nil.*
Paratyphoid bacilli.	"	Not so motile as bacillus typhosus but more so than bacillus coli.	Variable.	"	"		A, Usually no change. B, Sometimes fluorescence.	Paratyphoid A produced acid like bacillus typhosus and Paratyphoid B produced alkali.	Variable.	*Nil.*
Bacillus coli communis.	Shorter and thicker than bacillus typhosus.	Motility is not so marked as bacillus typhosus.	2-6.	More opaque than bacillus typhosus.	Whiter, thicker, more opaque, and showing gas bubbles.	Indol production marked.	Canary yellow colour produced and gas bubbles.	Marked acid and clot.	In 48 hours distinct brownish film which rapidly spreads and becomes thicker.	*Nil.*

* In addition to the culture media and other tests shown in the table the effects of Gram's stain, bile salt broth, mannite nutrose broth, raffinose nutrose medium, salicine nutrose medium, caffeine medium, and agglutination with enteric fever serum were also tried. The effects were as follows. *Gram's stain:* "decolorised" with all nine bacilli. *Bile salt broth:* "acid, no gas" for the first eight bacilli; "acid and gas" for the bacillus coli communis. *Mannite nutrose broth:* "unchanged" for the first five bacilli; "growth and acid" for the pseudo-dysenterial bacillus; "acid" for the last three bacilli. *Raffinose nutrose medium and also salicine nutose medium:* "acid and growth" for the pseudo-dysenterial bacillus; "unchanged" for the other eight bacilli. *Caffeine medium:* "growth" with the bacillus typhosus abdominalis and the paratyphoid bacilli; "no growth" with the other seven bacilli. On testing with enteric fever serum the agglutination result was "marked" with the bacillus typhosus abdominalis and "*nil*" with the other eight bacilli.

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following table summarises, according to this observer, the distinctive features of the two species:

Entamœba coli.	*Entamœba histolytica.*
No well-marked distinction between ecto- and endoplasm; latter stains more deeply.	Ectoplasm distinct; much more refractive and more deeply staining than finely granular endoplasm.
Rarely shows a vacuole.	Usually one or more non-contractile vacuoles.
Rarely contains erythrocytes, crystals or bacteria, etc.	Often contains large numbers of erythrocytes, crystals, bacteria, etc.
Nucleus sub-central and almost always visible; stains deeply; shows a well marked, rather thick and very refractile nuclear membrane; contains nucleolus and large amount of chromatin.	Nucleus excentric, small, usually indistinct; stains feebly; contains little chromatin, and has no marked nuclear membrane.
Motility very sluggish.	Motility more marked and definite.
Multiplication in the intestine by binary fission and, also, by multiple fission into eight amœbulæ. On fæces becoming hard, or outside the body, encystment and formation of eight amœbulæ which are set free when swallowed.	Multiplication in the intestine by fission and by a process of budding. On fæces becoming hard, or outside the body, formation without encystment of resistant spores, which develop when swallowed.

While many observers, partly as the result of their own work, but principally it would appear in deference to Schaudinn's great authority, have accepted these descriptions, there are others, notably Musgrave and Clegg, who declare, after careful work extending over several years and carried on in exceptionally favourable circumstances, that they fail to confirm Schaudinn's statements.

In the course of their work Musgrave and Clegg made many important discoveries having a bearing, not only on the ætiology but also on the prophylaxis of this type of dysentery. They claim to have shown that under certain conditions what apparently were non-pathogenic amœbæ, collected from a variety of sources, *i.e.* vegetables, water, etc., can be made to assume pathogenic properties. Further, following

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Frosch's methods, they succeeded in cultivating intestinal amœbæ by adding to the cultural media the bacteria usually associated with these amœbæ in the intestine, and which seem to exercise a necessary symbiotic or, rather, metabiotic action, *i.e.* modify the culture medium in a way favourable to the amœbæ. They have also shown that by gradual habituation amœbæ can be brought to withstand a degree of acidity greatly in excess of that normally present in the human stomach.

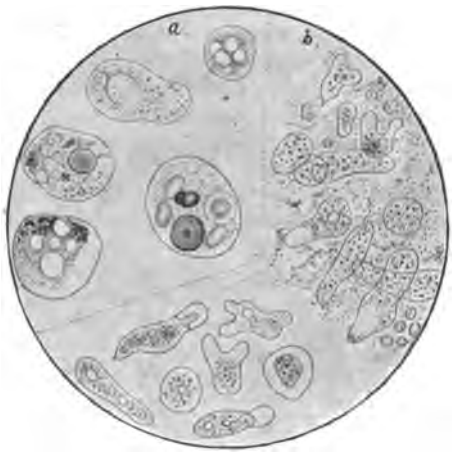

Fig. 61.—Amœba coli.

a, Amœba dysenteriæ fixed and stained (*Councilman*); *b*, A. dysenteriæ in stools (*After Lösch, Virchow's "Archiv," Bd.* 65).

When present in stools, the amœba (Fig. 61) is generally easy to find. All the preparation necessary is to pick out a small fragment of stool shortly after it has been passed, and then to lay this on the slide, and compress it sufficiently under the cover-glass to form a fairly transparent film. They are said to be most readily found in the watery stools produced by a saline purgative; doubtless because they are washed from off the surface of the bowel by the action of the drug. In hot weather a warm stage is

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not required; but in cold weather it is well, until the observer has become by practice familiar with the appearance of the parasite in its passive condition, to warm the slide. This, in the absence of more elaborate apparatus, may be conveniently done by placing the slide on a copper or tin plate with a hole cut in it to allow of the transmission of light. Such a warm stage should be provided with a long arm to the end of which a spirit-lamp is applied, care being taken not to raise the temperature of the slide above blood heat. Search is then made with a half-inch objective. The amœba is a clear, faintly greenish-tinted, transparent body, some three to five times the diameter of a red blood corpuscle. It is recognised by its movements, which closely resemble those of the ordinary fresh-water amœba. The faintly granular endosarc surrounded by the very clear ectosarc are distinguishable. The nucleus may sometimes be detected in the endosarc, as well as one or two non-contractile vacuoles, and, generally, various extraneous bodies such as blood corpuscles, bacteria, and so forth, which the amœba has included. As the temperature of the slide approaches blood heat the amœbæ send out and retract rounded pseudopodia. These when first protruded consist of ectosarc only; but when the clear protusion of ectosarc has been extended a little way the endosarc is seen suddenly to burst, as it were, and flow into it. If the temperature of the slide be allowed to fall below 75° F. the parasite will assume a sharply-outlined spherical form and remain quite passive until the slide is again warmed up, when the creeping movement may be resumed. In certain specimens heat fails to induce movement, the amœba remaining spherical and passive. The parasite will keep alive on the slide and exhibit movement for an hour or longer.

There can be no question as to the occurrence of this parasite in certain cases of dysentery, but it is not so easy to determine its exact significance in relation to the disease. It is found not only in the mucus lying on or thrown off by the inflamed bowel, but also in the sloughs on the ulcerated surface, in the

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tissues constituting the base and sides of the ulcer, and in the still living and relatively healthy tissues for some distance around the lesion. This intimacy of association constitutes a good *primâ facie* reason for regarding the parasite as the cause of the disease. On the other hand, there are many cases of dysentery in which the amœba cannot be found; cases, too, of relapsing dysentery with clinical characters such as are described as belonging to amœbic dysentery. Moreover, as is well known, the amœba, or an amœba hard to distinguish from *Amœba dysenteriæ*, is found in perfectly healthy stools, in cases in which there is no reason whatever to suspect the existence of disease of the alimentary canal.

Thus the occurrence of amœbæ in the stools of healthy individuals and their absence from the stools in a proportion of cases possessing the clinical characters of the type called "amœbic," suggest caution in definitely accepting the micro-organism as the true cause of this type of dysenteric disease, and the suspicion that after all it may be merely an epiphenomenon.

Gasser, in material supplied by 153 cases of dysentery—principally soldiers from Oran—although he found *Amœba coli* in 45 out of 109 acute cases, observed no relationship whatever between the number of amœbæ present in the stools and the severity of the disease. In 34 chronic cases he found the amœba in 13; and in 8 cases of chronic diarrhœa supervening on dysentery he found it in 5. In the stools of 20 healthy individuals from Oran he found the amœba in 4. He further states that he failed to find, or to recognise, the amœba in stained sections of dysenteric bowel. He concludes, therefore, against the amœba having anything more than an accidental relationship to the disease; that, in place of the amœba causing the dysentery, it is, if anything, the dysentery which causes, or rather, favours the amœba; in other words, that the amœba finds in dysenteric discharges a favourable medium for multiplying in.

Celli and Fiocca studied the parasitology of dysentery in material from 62 typical cases—some from Italy, some from Egypt. They, too, conclude that *Amœba coli* is not a direct cause of dysentery, and for the following reasons:—(*a*) Epidemic, endemic, and sporadic dysentery may occur without amœbæ in the stools. (*b*) Dysentery may be induced by the ingestion, or by the injection into the bowel, of dysenteric fæces which have been ascertained by microscopic examination

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to be quite free from amœbæ. (*c*) Amœbæ are very common in countries in which dysentery occurs, hence their frequency in the stools of dysenterics in these countries; they are there accidentally. They further point out that *A. coli* is not the only amœba to be found in the intestine; *A. guttula, diaphana, vermicularis, oblonga* and *reticularis*, besides *proteus*, have all been found there. *A. coli* has attracted attention, they consider, principally on account of its movements and size; whereas the other amœbæ, with perhaps quite as good a claim to be considered pathogenic, inasmuch as they can be detected only in specially-prepared cultures, elude the eye, even of the sharpest observer, in stools prepared in the ordinary way.

Many attempts have been made to induce dysentery by the injection of animals, or by feeding them with material—stools, liver pus, cultures—containing amœbæ. In a proportion of instances, especially where injections were used, amœbic dysentery has resulted. But as it is impossible to secure the amœba in pure culture, unless it may be in liver pus, these experiments are open to the objection that the successes depended possibly not on the amœbæ present, but on other micro-organisms of pathogenic origin unavoidably introduced at the same time.

Especially important, if its validity is established, is one of Schaudinn's experiments. It has a very distinct bearing on the way in which dysentery may be acquired under natural conditions, and as indicating the necessity for the immediate disinfection or destruction of dysenteric stools. Schaudinn fed cats on fresh dysenteric stool without inducing disease; but when he carefully dried the stools at natural temperatures, that is to say, when he had induced the *Entamœbæ hystoliticæ* they contained to form encapsuled spores, and then administered the material to cats, he produced typical amœbic dysentery. In other words, the amœbæ in fresh stool, being in their unprotected vegetative state, were destroyed by the gastric juice; but their resistant spores in dried stool, not being affected by this secretion, passed on to develop in the lower bowel.

The intimate connection of abscess of the liver with dysentery, and the presence of amœbæ in the contents of a large proportion of liver abscesses, are

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now well-ascertained facts which, to my mind, constitute a powerful, though by no means conclusive argument for regarding the amœba as an ætiological element, if not the probable cause, of amœbic dysentery.

There is yet another circumstance in connection with liver abscess which is not without significance. In a large proportion of liver abscesses the usual pyogenic bacteria are absent. This has been proved over and over again. Cultures made with such pus generally remain sterile. It is a very suggestive coincidence that it is just in those forms of suppurative hepatitis in which the usual pyogenic organisms are absent that this other parasite is present. Moreover, a liver abscess is not like ordinary abscesses; it has no proper abscess wall. Liver pus is not like pus elsewhere; it contains proportionately very few pus corpuscles; but it contains much tissue *débris*, many blood cells, and much granular matter. As an abscess it is altogether peculiar. A peculiar effect suggests a peculiar cause.

Anyone who has watched the movements of amœbæ on the warm stage can readily understand how such an organism might break down and separate the anatomical elements of a friable organ like the liver, and so cause a softening—a cavity resembling an abscess. It feeds on the tissues, in fact, and to grow and multiply it must disintegrate their structures and consume their cells. Amœbæ occur much more frequently in liver abscess than is generally supposed; a circumstance strengthening the argument for regarding this parasite as being in causal relationship to that lesion, and therefore, *pro tanto*, to dysentery.

BALANTIDIUM DYSENTERY.

The occasional occurrence of *Balantidium coli* in the fæces, particularly in association with dysenteric diarrhœa, has been recognised for the last fifty years. It is only lately, and more particularly since Strong and Musgrave called attention to the subject, that it has come to be regarded as the germ cause of a particular type of colitis, resembling in

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many respects amœbic dysentery. The parasite has been studied zoologically more especially in temperate climates, but it seems probable that extended observation will show that the balantidium is equally, if not more prevalent in warm climates.

Balantidium coli is an oval-shaped ciliated infusorian measuring 0·07 to 0·1 mm. by 0·05 to 0·07 mm. Its anatomical characters may be gathered from the accompanying illustration. It reproduces by division, budding and conjugation. Occasionally, losing its cilia, it may become encysted.

How it attains the human intestine is not known, but as it is a common parasite of the pig it is likely that this animal is a usual source of infection. As attempts to infect animals experimentally have failed, it is reasonable to conclude that the infusorian, on occasion, assumes some resistant form which enables it to withstand the gastric and intestinal juices on the way to its habitat, the end of the ileum and the large intestine. Although it may live for a considerable time in water or fæces (1 hour to 3 days), it has not been grown on culture media. Strong considers that cultures might succeed if made in association with certain bacteria, as in the case of *Amœba coli*. In liquid stools the balantidium exhibits great activity, indulging in locomoting as well as in rotary movements.

Fig. 62.—Balantidium coli.

The symptoms of balantidium dysentery are, in the present state of knowledge, indistinguishable from those of other forms of dysentery. The disease is chronic in type, its special nature being discoverable only on microscopical examination of the stools. Generally only one or two balantidia are found, but as many as twenty may be seen at a time in every field of the microscope.

In the large number of cases collected from different authors by Strong, together with those observed by himself, the mortality amounted to about 30 per cent. How much of this was due to the parasite and how

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much to concurrent and independent disease it is difficult to state.

In 30 cases in which autopsies have been made a variety of dysenteric lesions, from catarrhal congestion and diphtheritic patches to extensive ulceration, have been found. On section Strong demonstrated the balantidium not only in exudate on the surface of the bowel, but congregated in large numbers in the follicles, and imbedded in the tissues forming the base of the ulcerations, including submucosa and muscular coat, and even in the lumen of blood vessels and lymphatics.

The germs of dysentery water-borne.—Notwithstanding the vast amount of speculation, time and work expended in endeavouring to ascertain what the germ or germs of dysentery may be, it cannot be said that as yet we are even near the complete solution of the problem. One thing, however, is fairly well ascertained, and that is that these germs are often introduced by means of drinking water. The statistically-ascertained improvement in the public health in respect of dysentery in such large towns as Calcutta and Madras following so closely on the introduction of improved water supplies, and the improvement in the health of the British Navy following the introduction of regulations requiring that in all places in which the water supply is not above suspicion the drinking water served out to the men shall be distilled, constitutes powerful testimony in favour of regarding dysentery as a water-borne disease. This conclusion receives additional support from the occurrence of epidemics of dysentery in the crews of ships which have watered at polluted sources, as well as from the occurrence of similar epidemics in large institutions in which, by some accident, surface water has leaked into the water supply. This does not exclude the possibility of other sources of infection such as privies, dust, flies, and fouled vegetables, and the vessels or instruments used by dysenterics; but the water theory probably covers the vast majority of dysentery epidemics, as well as of sporadic cases.

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Predisposing and exciting causes. — It seems not improbable that, in conditions of sound health, the pathogenic organisms of dysentery may exist in and pass through the alimentary canal without attacking the tissues or giving rise to disease. So long as the mucous surface is sound and vigorous, it probably has the power of protecting itself against many such organisms. It is very probably the same in this respect with the dysentery germ or germs as with the cholera vibrio. Probably it is only on the establishment of some condition of lowered vitality, such as may be induced by catarrhal troubles, chill (a powerful excitant of dysentery), irritating food, bad food, constipation, malaria, scurvy, starvation, and so forth—all well-recognised exciting causes —that the dysentery germ can overpower the natural protective agencies and light up the specific lesions. It is a well-known fact that it is in such circumstances that dysentery is most apt to declare itself. Hence the importance of avoiding these things in tropical climates, more especially in the presence of a bad water supply or of an epidemic.

The capacity for latency often exhibited by the germs of dysentery, as of some other intestinal germs, sprue for example, is remarkable. I have encountered cases in which a dysenteric infection (amœbic) contracted in the tropics did not manifest itself for several months after the patient had returned to England. I have also encountered dysenteries that recurred in England at intervals of one and two years after infection, originally acquired in Egypt.

Influence of age, sex, and occupation.—All ages are subject to dysentery, children especially. Occupation has no special influence. Both sexes are liable. Pregnancy, miscarriage, and the puerperal state are grave complications.

Diagnosis.—Provided reasonable care be exercised, diagnosis, especially in acute cases, is usually easy. In chronic cases the question of seat worms, hæmorrhoids, polypus, stricture, tubercle, malignant and specific disease, proctitis, ulceration, abscess about the rectum, and tumour in the bowel, may require to

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be considered. Diagnosis must never be taken for granted. In every case stools must be inspected; and in every case in which there is any probability of rectal disease, some of the forms of digital or specular examination must be made. In African and West Indian cases the possibility of bilharzia disease of the rectum must be borne in mind, and a microscopical examination made of the urinary sediments and of the fæces with a view to the detection of any ova of bilharzia which may be present. So, too, in cases from the Far East, *S. japonicum* must not be forgotten. In children, especially, intussusception may occur independently, or as a complication of dysentery; the possibility of this must not be overlooked. Chronic dysentery is often diagnosed chronic diarrhœa. This error will be avoided by careful inquiry into the early history of the case, the detection of mucus, of amœbæ, of leucocytes or of red blood corpuscles in the stools, and the occurrence of tenesmus. Careful inquiry for any history there may be of occasional exacerbations in which straining, and blood and mucus in the stools, are more or less prominent features, will often lead to a correct diagnosis.

Treatment. — The treatment of dysentery requires much judgment and very careful supervision. In former days it was the fashion to bleed repeatedly and to a large amount, and at the same time to administer large doses of calomel—amounting in the aggregate to ounces—and of opium. It is not to be wondered at, therefore, that in those days the mortality was excessive.

Nowadays better and more rational methods prevail. There is less confidence in drugs, more in the self-recuperating powers of the body. A most important part of our modern plans has for its object to afford the diseased organs favourable conditions for repair; not so much to endeavour to heal them, as to give them the opportunity of healing themselves.

If called on to treat a case of what appears to be dysentery, our first duty is to assure ourselves that diagnosis is correct. We must inspect the stools, and,

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until the case is quite recovered, we must inspect them daily or frequently. Their condition is the surest guide in the management of this disease. From them we can form a fairly accurate idea of what is going on in the bowel, and from them we can judge of the effects of diet and of drugs.

Importance of rest.—It is with an inflamed bowel as with an inflamed joint: the first and all-important indication to fulfil is, after removing the causes of irritation, to place the part at rest. Could these two indications, the removal of the cause of irritation and the repose of the organ affected, be fulfilled thoroughly, repair would at once set in. Unfortunately, the affected surface being so inaccessible, we cannot always remove the irritant in the case of dysentery, nor can we place the parts involved at absolute rest. We can, however, partially meet these indications—quite sufficiently, as a rule, to insure recovery.

The diagnosis of dysentery established, the patient should at once be sent to bed. This in itself has a marked influence on the bowel. Repose must be as nearly complete as possible. The patient must not be allowed to get out of bed; when he has a call to stool he must use the bed-pan. To a certain extent this enforcement of rest is comparable to the placing of an inflamed leg in a splint and elevating it. It insures some degree of mechanical rest, and relieves the blood-vessels of the inflamed part of a certain amount of hydrostatic pressure.

Food in acute dysentery.—The indication of rest we further endeavour to meet by stopping all solid food. Were it possible, it would be well to stop all food. This, of course, is impossible, and so we make a compromise between the therapeutical indication and physiological necessity by reducing the diet to a minimum and selecting only such foods as, while possessing considerable nutritive value, yield but a small or non-irritating fæcal residue. The tongue is a fair index to the sort of food most likely to suit the case. When this organ is coated, indicating gastric catarrh, small quantities of thin

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chicken soup, egg albumin, thin barley- or rice-water, are better borne than milk; when the tongue is or has become clean, then milk, pure, diluted with barley- or rice-water or peptonised, is the best diet. Alcohol is generally contra-indicated, but in cases of collapse small feeds of white wine whey may be given with advantage. These foods should be taken in small quantities at a time, a little every hour or two. They must be given neither hot nor cold, as food when either too hot or too cold is apt to excite peristalsis and to cause colic and straining.

Malaria and scorbutus.—If upon inquiry it is found that there is reason to suspect either a malarial or a scorbutic element in the case, treatment must be modified accordingly. Careful practitioners never forget to ascertain if these important complicating elements are present or not. If malaria be suspected, or if temperature is markedly raised, it is well to make a careful microscopic examination of the blood for the parasite; if this is found, then quinine must be freely administered either by the mouth or, if the bowels are very irritable, by intramuscular injection. The presence of scorbutus, of course, indicates fruit juices and fresh unboiled milk, in addition to the usual treatment for dysentery.

Drug treatment.—A dose of castor oil and laudanum is a good preliminary in the treatment of dysentery; indeed, many cases are promptly checked thereby, and require no further treatment beyond rest and dieting for a day or two.

The drugs which have proved of most service in the treatment of severe dysentery are ipecacuanha, one or other of the aperient sulphates either of magnesium or of sodium, opium, and calomel. It is difficult to prognosticate in any given case whether ipecacuanha is likely to prove the more effective drug, or whether the sulphates, or calomel will answer better. In every case one or the other ought to be exhibited at once; one failing after a fair trial, the other unless manifestly contra-indicated, should get a chance.

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Ipecacuanha.—In English practice ipecacuanha is generally the first to be tried. It must be given on an empty stomach. The best plan is to interdict all food for three hours; then to give ten or twenty drops of laudanum in a tablespoonful of water and, at the same time, to apply a mustard poultice to the epigastrium. About twenty minutes later, when the patient is coming under the influence of the laudanum, twenty to thirty—some give as much as sixty—grains of ipecacuanha in pill, bolus, capsule, or in suspension in about half a wineglassful of water, are administered. With a view to prevent vomiting, the patient is directed to lie flat on his back, using a low pillow, and not to eat, drink, speak, or move for at least four hours. Probably he will fall asleep. Should he feel nauseated, he must as much as possible resist the desire to vomit. With the same object in view, when saliva begins to collect in the mouth, as it is apt to do in such circumstances, it must not be swallowed; on a slight sign from the patient the nurse should remove the accumulating saliva with a handkerchief. If much saliva be swallowed, it is sure to provoke vomiting. In some instances these precautions suffice to avert emesis. Should, however, the ipecacuanha be brought up within an hour of its being swallowed, the dose had better be repeated so soon as the nausea has subsided, the same precautions against vomiting being observed.

After six or eight hours, and when all feeling of nausea has subsided, small quantities of food may be given, and frequent and fractional feeding persisted in for six or eight hours, or until the following day, when the dose of ipecacuanha must be repeated. In many instances one or two such doses abort the dysentery, and the acute symptoms rapidly subside. It is wise, however, to go on with the ipecacuanha once or twice a day for at least a week or longer. It is a good practice to reduce the ipecacuanha by gr. v. every day. If the drug is doing good, copious feculent pultaceous yellow stools will be passed after a day or two. This diarrhœa must not be checked or regarded as an indication for stopping the drug.

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Ipecacuanha *sine emetinâ* may be tried; generally speaking it is unsatisfactory.

Aperient sulphates. — Should ipecacuanha appear to be doing no good, sodium sulphate—which is less irritating than magnesium sulphate—may be tried; indeed, by some this line of treatment is preferred from the outset. These salts have the advantage over ipecacuanha of not causing nausea, and they are often successful. They may be given in drachm doses in a little hot water, or in cinnamon water, every quarter of an hour until a purgative effect is produced, or they may be given in a large dose—half an ounce—to begin with, followed up by smaller doses if necessary. These large doses must not be given when the patient is feeble or in any sense collapsed. Buchanan, speaking from a large experience of dysentery (bacillary) in Indian gaols, recommends one or two teaspoonfuls of the following stock mixture every one or two hours until free gentle purgation is produced. It should then be continued sufficiently often to secure gentle purgation, and for one or two days after the mucus and blood have disappeared.

℞ Magnesii sulphatis	ʒij.
Acidi sulphurici dil.	ʒiij.
Tinct. zingiber.	ʒiij.
Aquam ad	ʒviij.

If the stools become watery the mixture must be stopped at once. The lessening of tenesmus and the production of copious, soft, feculent stools is the test of the successful action of the sulphates.

Calomel.—Should these means fail to control the disease, and should the bloody mucoid stools persist, and the griping and tenesmus continue, recourse may be had to calomel in combination with opium and ipecacuanha—a grain of each every five or six hours, the effect being watched and salivation avoided. Some give calomel from the outset as a routine treatment in dysentery, either in five-grain doses every six or eight hours, or in fractional doses every hour. This method is most in vogue in Germany, and is probably best suited to the croupous forms of the

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disease. In France and the United States the sulphates are most in vogue; while British physicians until lately, relying on Indian experience, place most confidence in ipecacuanha.

Bismuth and opium.—As a result of either line of treatment, the dysenteric symptoms may subside rapidly—perhaps entirely. Sometimes, although the stools become feculent, and the mucus and blood disappear, diarrhœa remains. This generally quickly yields to a salicylate of bismuth (grs. x–xx) and morphia (gr. $\frac{1}{12}$) mixture.

Other drugs.—*Simaruba* (*Ailanthus glandulosa*) sometimes succeeds where other measures have failed. It is a drug which, though nowadays neglected in Europe, is still much used in the East by so-called "dysentery doctors." It seems to be specially serviceable when the case has become subacute or chronic. To be effective, it requires to be given in much larger doses than is directed in the Pharmacopœias. One method of preparation I have seen employed is as follows:—Using an earthenware pot, boil half an ounce of simaruba in a pint and a half of water for three hours, and then strain it. Let the patient remain in bed and drink this decoction on an empty stomach every second morning for four times. Food must consist of milk and farinaceous stuffs. Another method is to boil an ounce of simaruba in twelve ounces of water until it is reduced to seven drachms; to this a drachm of spirit is added. This preparation, also, must be made in an earthenware, or in an enamelled, dish. For an adult this is a suitable dose; a child may take a fourth part. It should be taken every night for four nights.*

* The following is the formula of a preparation of simaruba much used in Shanghai, and there known as "Rhein's Specific Remedy for Diarrhœa and Dysentery." I understand that the formula was purchased by the Shanghai municipality for a considerable sum of money, so highly was it thought of by the European community of that city. Simaruba bark, three ounces; Chinese cinnamon, one ounce; boil in three quarts of water and allow it to evaporate down to one pint. When cool, strain into a brandy bottle, add three tablespoonfuls of good brandy, and fill up by pouring cold water over the bark in the strainer till the bottle is full. Dose: A wineglassful three times a day.

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Monsonia ovata.—Maberly reports favourably on *Monsonia ovata*—a South African plant—in dysentery. He uses a tincture of two and a half ounces of the dried plant to the pint of rectified spirit. It gave in his hands wonderful results, both in acute and in chronic cases which had resisted the ordinary remedies.

Cinnamon, pomegranate, mangosteen rind, and other aromatics and astringents sometimes do good in chronic dysentery.

I can offer no explanation of the action of any of these drugs in dysentery. We use them quite empirically. Ipecacuanha and simaruba really seem to have some sort of specific action on the disease or on its cause, but in what way it is impossible to indicate with certainty. I incline to think that ipecacuanha has a specific action on the amœba, comparable to that of quinine on the malaria parasite or mercury on the spirillum pallidum, and that in this way it changes a specific into a simple inflammation. The special rôle of this drug I consider to be amœbic dysentery. Strange to say, ipecacuanha, which has been found so serviceable in India, Africa, the Brazils and elsewhere, has a very poor reputation as an anti-dysenteric in the United States (Osler); it has also signally failed in some English epidemics (Clouston); facts pointing to specific differences in the dysenteries of different countries.

Relief of pain.—During the early stages of an attack the patient may suffer much from griping and tenesmus. These are generally relieved by hot fomentations, turpentine stupes, or by a hot bath. An excellent application is the Japanese hot-box or hand-warmer—a small tin box containing a slowly-burning cartridge of powdered charcoal. These hot-boxes, or an imitation under the name of "istra," can now be procured in England. Three or four of them may be roughly sewn into a piece of flannel and laid on the abdomen. This application has the advantage of being very light, of not wetting the clothes, and of keeping warm for many hours. Tenesmus and dysuria are best relieved by morphia hypodermically;

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or by an enema of a wineglassful of thin starch containing forty or fifty drops of laudanum; or by suppositories of morphia and cocaine. Washing out the rectum with a pint of very hot water, with or without boracic acid, is sometimes effectual in removing for a time, or, at all events, of mitigating the incessant desire to go to stool and to strain. Two drachms of bismuth with laudanum thirty minims, and thin starch two ounces, is also a good sedative enema (Davidson).

Treatment should be energetic and thorough at the outset of dysentery. Every effort must be made to prevent it from becoming chronic, as in this stage the disease is very difficult to treat successfully, and is prone to issue in permanent invalidism.

Treatment of chronic dysentery.—As a matter of routine my personal experience leads me to recommend in all cases of chronic amœbic dysentery a preliminary course of ipecacuanha—30, 25, 20, 15, 10 and 5 grains on successive evenings, with, of course, rest and a milk and barley-water diet. Thereafter I generally prescribe a minute dose of castor oil, with or without opium, three times a day, regulating the dose according to effects. I may also prescribe a mixture of simaruba and cinnamon, or some intestinal antiseptic, as salol or β-naphthol. Sometimes I continue the ipecacuanha in 5 grain doses for a month or longer, regarding it as a specific which should be persisted with as we would when giving quinine, iodide of potassium, or mercury. These measures failing, I have recourse to some of the following.

Nitrate of silver injections.—The most effective treatment of certain types of chronic dysentery is undoubtedly injections of large quantities of nitrate of silver solution of a strength of from half a grain to one grain to the ounce of distilled water. There is a right and there is a wrong way of using this splendid remedy. If employed in the wrong way, it is useless; perhaps worse than useless. It must never be applied when acute symptoms are present. These must first be got rid of by ipecacuanha, by the

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sulphates, by calomel, by castor oil, and by rest and diet. The patient should be prepared for a week at least in this way. Then the bowel is to be cleared by a small dose of castor oil, followed by a large enema of three or four pints of warm water to which two or three teaspoonfuls of carbonate of soda have been added. The whole of this injection having escaped, and when the bowel is quite empty, two to three pints of the nitrate of silver solution are thrown in by means of a long tube passed slowly and carefully into the bowel as far as it will go without kinking. It is better to fill the bowel by gravitation, using a funnel and tube, rather than by a syringe. If it seems to be doing good, this injection may be used every few days and kept up for some time. Improvement in suitable cases generally sets in at once. The nitrate, or any other form of enema, must not be persevered with if it causes any marked irritation or increase of symptoms.

In the mild chronic dysenteries which are seen in Great Britain, and which originally had been contracted in the tropics, and also in the more acute relapses of tropical dysenteries, ipecacuanha should always be tried in the way recommended.

Other methods of treating chronic dysentery which succeed at times are the systematic washing out of the bowel daily with warm boracic water, with linseed infusion, with milk (a very valuable remedy), with mangosteen rind decoctions, with weak solutions of alum, sulphate of copper, or tannin, with hypochloride of soda solution 1%, with creosote and water or milk—a teaspoonful to the quart; systematic daily dosing with small quantities of castor oil, with or without opium—one to two drachms of castor oil with four to ten drops of laudanum three times a day (Hillier); ten to twenty drops of turpentine three times a day; small doses of hydrarg. c. cretâ; the daily consumption of some preparation of fresh bael fruit; a course of Carlsbad, of Kissingen, or of Vichy water; rectal douching as practised at Plombières; a diet of grapes only, of milk only, or of beef only; cold water compresses to the abdomen.

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Surgical treatment of chronic dysentery.—When less heroic methods fail and the patient's condition is slowly but progressively deteriorating, right inguinal colotomy, or appendicostomy should be offered as affording a reasonable chance. Some time ago I had a colotomy performed in such circumstances with excellent results. If so serious an operation is declined, appendicostomy might be urged. This is easily performed and is not so risky or troublesome as colotomy. A small oblique opening is made through the abdominal wall at the spot usually selected for appendicectomy. The opening should be large enough to admit two fingers and the appendix is hooked out; this is easy, if no adhesions are present. The appendix is drawn through the wound until its base is in contact with the parietal peritoneum, and it is then fixed in this position by a fine stitch of silk or catgut passing through the meso-appendix and the adjacent edges of the peritoneum. The appendix is opened immediately or in a few days' time. The cæcum and colon may now be washed out as frequently as desired through the appendicostomy opening. For this purpose a No. 8 rubber catheter with a copper stylet is employed, and a rectal tube with an outflow tube. The patient lies on his back, but if the cæcum gets distended and the fluid does not pass, turning him slightly to the left will restore the flow.

Post-dysenteric constipation.—After the subsidence of a dysentery, constipation and balling of the stools is by no means an uncommon event. This complication is best prevented, or met, by enemata of warm water to which a little salt—a teaspoonful to the pint has been added—or, if the bowel is very irritable, of linseed tea or of thin rice-water. An occasional dose of castor oil, half to one teaspoonful, once or twice a week or oftener, and kept up so long as the motions are not quite healthy, is an excellent routine practice; its action may be supplemented by a glycerine suppository. A course of Carlsbad waters or salts often gives excellent results.

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Food and clothing.—In chronic dysentery much attention should be given to clothing and food. The former should be very warm. Dysenterics ought never to feel cold. Cold bathing is very dangerous for them; so are alcoholic drinks of all sorts. Food should be simple in the extreme. Beef, mutton, cheese, bread, coarse fruit or coarse vegetables, nuts, pickles, and such-like are, as a rule, not well borne. Fruit and fine well-cooked vegetables in moderation are necessary and often beneficial. In obstinate chronic dysentery it is often a good thing to change the diet from slops to solids, from a meagre to a more liberal one. The quantity of food is as important as the quality. Chronic dysenterics should eat no more than suffices to maintain their weight. Large meals must be avoided, and food should not be taken unless there is appetite. Wonderful results are sometimes got from a sea voyage.

Hepatitis.—During the whole course of an attack of dysentery, and for months thereafter, the condition of the liver must receive the most careful attention. We may not be able to prevent abscess of this organ; but if pain and swelling seem to suggest it as threatening we can try by means of full and repeated doses of ipecacuanha, saline aperients, rest, low diet, fomentations, dry cupping, and such-like measures to avert what, to say the least, is a very grave complication.

Prophylaxis.—The prophylaxis of dysentery consists principally in securing a pure water supply; in avoiding unwholesome food; in temperance; in clothing warmly and avoiding chill; in correcting constipation and stopping diarrhœa; and, in public institutions such as gaols and asylums, in regarding dysentery as an infectious and readily communicable disease, and in strictly isolating all patients suffering from symptoms of colitis, or even looseness of the bowels.

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CHAPTER XXVIII

EPIDEMIC GANGRENOUS RECTITIS

So far as known, this very fatal disease seems to be confined to the natives of the low-lying, hot, damp regions in the north of South America, and, perhaps, to the natives of Fiji and other islands of the South Pacific. In Guiana it is known as "Caribi" or "Indian sickness," in Venezuela as "Bicho" or "El Becho." It is said to be very contagious, and appears to be a form of rapidly-spreading phagedæna, which starts from the neighbourhood of the anus. Occasionally it may begin higher up—in the colon. In the latter case it is called the "high" form; in the former the "low" or rectal form. Animals, as well as men, are attacked.

I am indebted to Dr. Ackers, of Curaçoa, formerly of Venezuela, for the following information on the subject:—"I have only seen cases of the disease in animals, principally fowls, though also in dogs and calves; but I have been told by medical men, who themselves attended the cases, of its occurrence in children of the poorer classes. The disease commences by an itching in the anus, which produces an inclination to frequent defæcation. This stage continues for a few days, when a severe inflammation of the mucous membrane of the rectum sets in, giving rise to symptoms of acute dysentery. There are frequent stools of a mucous, bloody substance, accompanied sometimes by bile or excrement; at the same time, there is much straining, considerable elevation of temperature, anorexia, and great thirst. At this period, if the animal or child is not attended to, the above symptoms become more alarming; a constant flow of a slimy, fœtid, semi-liquid substance streaked with blood appears. Sometimes the discharge is of a bright green colour, such as might be obtained by

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crushing tender stalks of grass. When this occurs the patients refuse all food, but the thirst is still intense. The affected animal remains standing in one place, with drooping head, as if overcome by fever and weakness. For a day or so it continues like this, until at last, unwilling to move, eat, or even drink, it suddenly dies in convulsions. Sometimes, however, this stage is not fatal, but is followed by prolapsus of the rectum, which is in a very inflamed state and ulcerated; rapidly gangrene sets in and is quickly fatal. The Venezuelan peasants state that this disease arises in children from chewing the green tender stalks of unripe maize, of which they are very fond on account of its sweetness. In children prolapsus of the rectum is very frequent; in bad cases they may die, like the animals, in convulsions, though in children convulsions are not necessarily a fatal symptom. The treatment employed by the natives for animals consists in an enema of strong lemon juice, mixed with a weak dilution of white rum and water (aguardiente), two or three times a day; at the same time, the anus is freely dusted with wood ashes, some of which are also introduced into the rectum. A purgative of oil is generally administered also. In some cases I have known this treatment prove very successful. On the other hand, when the disease is far advanced, or when the ulceration of the bowel appears at an early date, it seems to be of little or no avail. Another treatment employed, especially for children, consists in an enema of the juice obtained by crushing the stalks and leaves of *Spigelia anthelmintica* (pasote). A decoction of the same herb is also given by the mouth three or four times a day. This decoction is very frequently administered by the peasants as an anthelmintic. In cases of children suffering from 'bicho,' one of the quarters of a lemon is roasted and introduced into the rectum as a suppository once or twice a day, and I have heard that it gives very satisfactory results."

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CHAPTER XXIX

HILL DIARRHŒA

Definition.—A form of morning diarrhœa accompanied by flatulent dyspepsia and the passage of copious liquid, pale, frothy stools. It occurs principally in Europeans on their visiting the hills after residing for some time in the hot lowlands of tropical countries.

Geographical and seasonal distribution.—Crombie, who gave an excellent account of this disease, pointed out that a similar affection may show itself in the highlands of Europe as well as in those of India. It is said also to occur in corresponding circumstances in South Africa and South America. There is no reason, therefore, to suppose that hill diarrhœa is special to India, although, owing to the large European population frequenting the hill sanitaria in that country, it has been particularly noticed there. An elevation of 6,000 feet or over, if combined with an atmosphere saturated with watery vapour, is particularly favourable to its development. In India it is found to begin and end with the rains, during which, in certain years and places, it is apt to assume almost epidemic characters. Thus, during the wet season of 1880, in Simla an epidemic of hill diarrhœa affected from 50 to 75 per cent. of the population, three-fourths of the cases happening within a week of each other. In some years hill diarrhœa is less prevalent than in others; but at the proper season few of the various hill sanitaria of India are without examples.

Ætiology and pathology.—It is difficult to say what may be the precise factors determining this disease. The low barometric pressure associated with great elevation above the sea-level may be a favouring circumstance. Damp seems to be indicated by the

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fact that the disease occurs principally during the rains. Chill after exposure to the high temperature of the plains has possibly an important share. Manifestly there is a suspension of the functions of the liver and, considering the dyspepsia and looseness, most probably of those of the pancreas and of the other glandular structures subserving digestion. Hill diarrhœa is certainly something more than an intestinal catarrh. As Crombie pointed out, it is more in the nature of dyspepsia. There are no adequate grounds for connecting it with either the water or the food supply. The question of micro-organisms has, apparently, not been studied.

Symptoms.—Without very obvious cause the patient, who in other respects may be in good health, soon after arrival at a hill sanitarium becomes subject to a daily recurring diarrhœa, the looseness coming on regularly every morning some time between 3 and 5 a.m. The calls to stool are apt to be sudden and imperative. The motions passed are remarkably copious; very watery in some instances, pasty in others. They are pale, frothy, and like recently stirred whitewash, so devoid are they of biliary colouring matter. Their passage is attended with little or no pain, often with a sense of relief. From one to half a dozen, or more, such stools may be voided in the morning before 11 a.m. After that hour, at all events in ordinary cases, the diarrhœa is in abeyance for the rest of the day, and the patient may then go about his duties or pleasures without fear of inconvenience.

The distinctive features of this form of diarrhœa are, therefore, the regularity of its recurrence every morning and its cessation after a certain hour in the forenoon; the absence of colour in the stools; and the attendant flatulence. The abdomen is sometimes blown out like a drum, the patient being conscious of unpleasant borborygmi associated with a feeling as of some boiling or chemical operation proceeding in his inside. Occasionally cases are met with in which the stools are very pale, although there is no diarrhœa.

Under treatment, or spontaneously, or, according to Crombie, on acclimatisation occurring, after some

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days or weeks the diarrhœa may subside. In other instances it persists in defiance of treatment until the return of the patient to the warm plains, when it at once spontaneously subsides. Crombie instanced a case in which the patient was regularly attacked with hill diarrhœa whenever he visited Simla—twelve occasions, recovery invariably taking place on his return to the plains. If the looseness is both considerable and protracted, there necessarily ensue debility, wasting, and anæmia, and the disease may lapse into confirmed sprue—an affection having, apparently, close affinities with hill diarrhœa.

Treatment.—The treatment recommended by Crombie, and endorsed by other medical men of experience in India, consists in a pure milk diet, rest, warm clothing, a teaspoonful of liquor hydrargyri perchloridi in water about fifteen minutes after food, and twelve grains of pepsine, or a corresponding quantity of lactopeptine or ingluvin, two hours later. If, in spite of treatment, the disease persists, the patient must return to the low country.

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CHAPTER XXX

SPRUE (PSILOSIS)

Definition.—By the term "sprue" is understood a peculiar and very dangerous form of chronic catarrhal inflammation of the whole or part of the mucous membrane of the alimentary canal, generally associated with disturbance of the chologenic function of the liver and, probably, of the functions of the other glandular organs subserving digestion. Although a disease of warm climates it may develop for the first time in temperate climates; only, however, in individuals who have previously resided in the tropics or subtropics.

Sprue is characterised by irregularly alternating periods of exacerbation and of comparative quiescence; by an inflamed, bare, and eroded condition of the mucous membrane of the tongue and mouth; by flatulent dyspepsia; by pale, phenomenally copious and generally loose, frothy, fermenting stools; by wasting and anæmia; and by a tendency to relapse. It may occur as a primary disease, or it may supervene on other affections of the bowels. It is very slow in its progress; and, unless properly treated, tends to terminate in atrophy of the intestinal mucosa, which usually, sooner or later, proves fatal.

Nomenclature.—Sprue has been more or less recognised by writers on tropical medicine for many years. It has been called "tropical diarrhœa," "diarrhœa alba," "aphthæ tropicæ," "Ceylon sore mouth," "psilosis linguæ" (Thin), besides a variety of other names. The term "sprue" is an adaptation from the Dutch word "spruw" in use in Java, where the disease is very common.

Geographical distribution.—It is probable that sprue, although more common in certain warm

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countries than in others, is found throughout the greater part of the tropical and many parts of the subtropical world. It is especially common in South China, Manila, Cochin China, Java, the Straits Settlements, Ceylon, India, tropical Africa, and the West Indies (Hillary). Apparently it is most prevalent in those tropical countries in which prolonged high temperature is combined with a moist atmosphere. It is common, however, in certain subtropical countries, as North China and even in Japan; countries where, although the summer is hot and damp, the winter is dry and bracing.

Ætiology.—Prolonged residence in the endemic area is, perhaps, the most potent predisposing influence; cases, however, do occur in which the disease shows itself after a residence of one or two years only. Exhausting diseases, particularly those involving the alimentary canal, as dysentery, hill diarrhœa, morning diarrhœa, hæmorrhoids and fistula, are apt to terminate in sprue. Frequent childbearing, miscarriages, uterine hæmorrhages, exhausting discharges, and prolonged lactation also predispose to the disease; so may syphilis, courses of mercury or of iodide of potassium, bad food, bad water, anxiety, chills, and so forth—in fact, any depressing influence, particularly if it is combined with intestinal irritation. Malaria does not seem to be specially responsible. At one time *Strongyloides intestinalis* (*Anguillula intestinalis*), a parasite very common in the stools of cases of chronic intestinal flux, particularly in Cochin China, was put forward as the cause of the chronic entero-colitis (for the most part sprue) of that country. Subsequent investigations have disproved this. Like the anguillula, *Amœba coli* or *Bacillus dysenteriæ* may be present in the stools in these cases; but, similarly, they are in no way responsible for the disease. Neither has any bacterium which can be regarded with any degree of certainty as special to sprue been separated from the characteristic stools. In searching for the fundamental cause of this affection, the latency which the disease occasionally exhibits, and the fact that the first symptoms may not appear until months or even

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years have elapsed since the patient quitted the tropics, must be kept in view.

Symptoms. — *Variability.* — There is infinite variety in the combination and in the severity of the various symptoms of sprue, as well as in the rate of progress of the disease. In some instances it may be almost a subacute process running its course in a year or two; in others, again, it may drag on intermittingly for ten or fifteen years. Much depends in this respect on the circumstances, the character, the care, the treatment, the age and the intelligence of the patient.

General symptoms in a typical case. — In an ordinary fully developed case the patient—who is generally dark or muddy in complexion and much emaciated—complains of three principal symptoms: soreness of the mouth, dyspeptic distension of the abdomen, looseness of the bowels; the last being particularly urgent during the morning and earlier part of the forenoon. The patient may also complain of feeling physically weak, of loss of memory, and of inability to take exercise or to apply his mind. His friends will probably volunteer the information that he is irritable and unreasonable.

Mouth lesions. — If the mouth is examined, the soreness will be found to depend on a variety of lesions of the mucous membrane, which, though painful, seem to be of a very superficial character. These lesions vary considerably in intensity from day to day. During an exacerbation the tongue looks red and angry; superficial erosions, patches of congestion, and perhaps minute vesicles appear on its surface, particularly about the edges and tip. Sometimes, from the folding consequent on swelling of the mucous membrane, the sides of the organ have the appearance of being fissured. The filiform papillæ cannot be made out, although here and there the fungiform papillæ may stand up, pink and swollen. If the patient be made to turn up the tip of the tongue, very likely red patches of superficial erosion, sometimes covered with an aphthous-looking pellicle, may be seen on either side of the frænum. On everting

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the lips, similar patches and erosions are visible; and if the cheek be separated from the teeth the same may be seen on the buccal mucous membrane. Occasionally the palate is similarly affected; very often in this situation the mucous follicles are enlarged, shotty, and prominent. The gullet and uvula may also be congested and, in places, raw and sore.

In consequence of the irritation caused by these superficial and exceedingly sensitive lesions, the mouth tends to fill with a watery saliva which may dribble from the corners. If the patient attempts to take any sapid food, strong wine, or anything but the very blandest diet, the pain and burning in the mouth are intolerable; so much so that, although perhaps ravenously hungry, he shirks eating. Not unfrequently swallowing is accompanied and followed by a feeling of soreness and burning under the sternum; suggesting that the gullet, like the tongue, is also in an irritated, raw, and tender condition. During exacerbations of the disease the condition of the mouth becomes greatly aggravated. Although during the temporary and occasional improvements it becomes much less painful, even then salt, spices, strong wines, and all kinds of sapid foods sting unpleasantly; and the tongue, particularly along its centre, is seen to be bare and polished as if brushed over with a coating of varnish. At all times the tongue is abnormally clean and devoid of fur; during the exacerbations it is red and swollen, but during the remissions, and when not inflamed, it is small, pointed, and, owing to the anæmic condition of the patient, it may be yellowish like a piece of cartilage.

Dyspepsia.—Dyspepsia is usually much complained of, the feelings of weight, oppression, and gaseous distension after eating being sometimes excessive. Very likely the abdomen swells out like a drum, and unpleasant borborygmi roll through the bowel. Occasionally, though not often, there may be vomiting, the vomiting sometimes being sudden and not always accompanied by feelings of nausea.

Diarrhœa.—The diarrhœa associated with sprue is of two kinds; one chronic and habitual, the other

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more acute and, in the early stages, evanescent. The former is characterised by one or more daily discharges of a copious pale, greyish, pasty, fermenting, acid, mawkish, evil-smelling material. The latter is of a watery character, also pale and fermenting, the dejecta containing undigested food and, usually, an abnormally large amount of oil and fatty acids. In these latter circumstances the diarrhœa usually brings with it considerable relief to the dyspeptic distension, at all events for a time. When the mouth is inflamed the diarrhœa is usually more active. The stools during periods of quiescence may be confined to one or two in the early morning or forenoon; during the later part of the day the patient is not disturbed. The stools, however, even in this quiescent phase, are always extraordinarily copious, the excessive bulk being attributable in great measure to the aforementioned excess of fat and the innumerable microscopic gas bubbles; patients remark their phenomenal abundance. They are passed almost, or altogether, without pain. Not unfrequently during exacerbations there may be a tender excoriated condition of the anus, and sometimes, in women, a similar condition of the vagina.

Types, history, course, and termination. Protopathic sprue.—There is a striking uniformity in the history of most cases of sprue. On inquiry, we shall probably learn that the patient has been suffering for months, or perhaps years, from irregularity of the bowels. This, we may be told, began soon after arrival in the tropics as a bilious morning diarrhœa. For a long time this morning diarrhœa went on, without interfering in any way with the general health. Later the mouth, now and again, became tender, little blisters or excoriations appearing for a day or two at a time about the tip of the tongue or inside the lips. These sore spots would come and go. Perhaps, from time to time, exacerbations of the mouth symptoms would be associated with a little increase of diarrhœa. Gradually the stools lost their bilious character and became pale and frothy; dyspeptic symptoms, particularly distension after meals, now

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appeared. As time went on, these symptoms would recur more frequently and in a more pronounced form, following, almost inevitably, any little imprudence as regards food or exposure. The general condition now began to deteriorate; emaciation, languor, lassitude, and inability to get through the day's work satisfactorily becoming more pronounced each summer until, finally, a condition of permanent invalidism was established. Should the disease continue to progress, the emaciation advances slowly but surely. Diarrhœa may be almost constant, and now no longer confined to the morning hours; the complexion becomes dark, sometimes very dark; the appetite, sometimes in abeyance, is more frequently ravenous, unusual indulgence in food being followed by increased discomfort, temporarily relieved by smart diarrhœa. Finally the patient is confined to the house, perhaps to bed. The feet become œdematous, and the integuments hang like an ill-fitting garment, the details of the bony anatomy showing distinctly through the dry, scurfy, earthy skin. Finally, the patient dies in a semi-choleraic attack; or from inanition; or from some intercurrent disease. Such is the history of an ordinary, mismanaged case of sprue.

Sprue secondary to dysentery.—When the disease has supervened on dysentery, we learn that the motions characteristic of the original dysenteric attack had gradually changed in character; from being scanty, mucoid, bloody, and accompanied with pain and tenesmus, they became diarrhœic, pale, frothy, their discharge being followed by a feeling of relief rather than of pain. The mouth at the same time became sore, exhibiting the characters already described. Gradually a condition of confirmed sprue was established, which ultimately, unless properly treated, will almost certainly prove fatal.

Sprue secondary to acute entero-colitis.—Another type of case commences as an acute entero-colitis with sudden and profuse colicky diarrhœa, vomiting perhaps, and a certain amount of fever. The acute symptoms do not subside completely, but gradually

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have the typical symptoms of sprue grafted on to those of an acute intestinal catarrh.

Incomplete sprue. (*a*) *Gastric cases.*—Occasionally we meet with cases of confirmed sprue in which, at first, the morbid process, judging from the existing clinical symptoms and subsequent history, is confined to a limited part of the alimentary canal. Thus we sometimes get sprue without diarrhœa, the principal symptoms being sore mouth, dyspeptic distension, pale, copious but solid stools, and wasting.

(*b*) *Intestinal cases.*—On the other hand, we may get cases in which the mouth is not eroded, and in which there is little or no distension or dyspepsia, but in which the stools are liquid, copious, pale, and frothy. Sometimes a patient who may have suffered at an earlier period, or on a former occasion from the first type of the disease, later acquires the diarrhœic form; and *vice versâ*.

(*c*) *Sprue without diarrhœa.*—It sometimes happens that under treatment the sore mouth, the dyspepsia, and the diarrhœa completely subside; nevertheless the wasting continues, the stools remaining phenomenally copious—so much so that the patient may declare that more is passed than has been eaten. In this case wasting is progressive, and the patient gradually dies of inanition.

Intestinal atrophy consequent on sprue.—In certain instances, under treatment the symptoms proper to sprue subside; but the patient's digestive and assimilative faculties are permanently impaired. Slight irregularities either in the quality or the amount of food, chill, fatigue, depressing emotions, and other trifling causes suffice to bring on dyspepsia accompanied by flatulence and diarrhœa. These cases may linger for years. Usually they improve during the summer in England, getting worse during the winter and spring, or during cold, damp weather. Ultimately they die from general atrophy, diarrhœa, or some intercurrent disease.

Morbid anatomy.—*Post mortem* the tissues in sprue are abnormally dry; fat is almost com-

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pletely absent; the muscles and the thoracic and abdominal viscera are anæmic and wasted. With these exceptions and certain important changes in the alimentary tract, so far as known there are no special lesions which are invariably associated with this disease. According to Bertrand and Fontan, occasionally certain changes are present in the pancreas—namely, fatty or granular degeneration of the cells, with softening of isolated acini and slight inflammatory infiltration of the connective tissue. These, however, are not more constant than are certain other and similar changes occasionally found in the liver and kidneys.

Lesions of the alimentary tract.—The principal and characteristic lesions are found in the alimentary tract. The bowel is thinned to such an extent as to be almost diaphanous. The serous coat is generally healthy, the muscular coat atrophied. The submucosa in places has undergone hypertrophic fibrous changes; and the mucous membrane from mouth to anus, either in patches or universally, is superficially eroded and interstitially atrophied. The internal surface of the bowel is coated with a thick layer of dirty grey, tenacious mucus which conceals patches of congestion, of erosion, or even of ulceration, besides such evidences of similar antecedent disease as pigmented areas and thin-scarred, cicatricial patches. The villi and glands are eroded and in many places completely destroyed. Here and there minute spherical indurations, about the size of a pin's head and surrounded by a dark pigmented or congested areola, can be felt in the mucous membrane. On cutting into these, they are found to be minute cyst-like dilatations of the follicles filled with a gummy, muco-purulent material. Sections of the diseased bowel show under the microscope corresponding changes; such as varying degrees of erosion or ulceration of the surface of the mucous membrane; degeneration of villi, glands, and follicles; the small mucous cysts referred to; sometimes small abscesses; and, also, infiltration by leucocytes of the basement membrane and submucous layer; and, in the latter,

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fibro-cirrhotic changes. The mesenteric glands are generally large and pigmented, perhaps fibrotic. The erosion lesions are usually most marked towards the end of the ileum and in the colon; but they may be present in greater or lesser degree universally, or in patches throughout the entire alimentary tract from mouth to anus.

Pathology.—In attempting an explanation of the phenomena of sprue, two features of the disease have to be considered—the catarrhal condition of the alimentary canal, and the absence of the normal colouring matter of the fæces. Possibly one of these is the consequence of the other; possibly the two conditions are concurrent but independent consequences of the same cause. What that cause may be is quite unknown. Whether the first pathological step originates in physiological exhaustion of the digestive functions, brought about by tropical conditions abnormal to the European constitution; or whether the disease depends upon a specific organism; or whether there is a combination of these, has still to be settled. In view of the occurrence of morning diarrhœa of dark bilious stools as a frequent first step in the development of sprue, hyperactivity of the liver might be assumed to be a first step in the development of the disease, an activity which in time ends in exhaustion of the chologenic functions of the gland. It might be further suggested that, concurrently with this hepatic disturbance, there is a similar initial hyperactivity of all the other glands appertaining to digestion, a hyperactivity which also ends in a corresponding exhaustion. Chemical changes in the ingested food would then follow on the establishment of these apeptic conditions, and ultimately, from the formation of acrid chemical bodies, lead to the chronic catarrhal changes found *post mortem*.

Analyses of the stools in sprue by Wynter Blyth, Hunter, V. L. Scheer, Harley and others resulted in ascertaining the presence of the ordinary elements of bile, notwithstanding their apparent absence so far as lack of colour would indicate. Bile is secreted,

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but the colouring matter, bilirubin, is not formed, or is changed in the intestine into a colourless substance. The excess of fat in the stools would indicate pancreatic disease or destruction of the lacteal capillaries.

Micro-organisms, of course, abound in the fermenting stools; but hitherto no bacterium or protozoon which could be regarded as specific has been found in association with the disease.

Personally, I incline to regard sprue as the result of a specific infection falling upon structures subserving digestion, exhausted by the over-stimulation by certain meteorological conditions unsuited to the European constitution. The remarkable effect of physiological rest, as supplied by "the milk treatment," in curing sprue, the rarity or absence of the disease in the natives of the endemic area, the occasional latency of the disease, and the tendency to relapse seem to support this hypothesis.

Diagnosis.—The condition of the tongue, the character of the stools, and the history are sufficiently distinctive, one would suppose, to render diagnosis an easy matter. Nevertheless, I have known of cases in which the disease has been diagnosed and treated as syphilis, the condition of the mouth being attributed to this disease, the character of the stools and other symptoms being ignored. Care must be exercised in interpreting the significance of the small area of liver dulness usually found in well-marked cases of sprue. This is not due to cirrhosis of the liver, but to the wasting this organ undergoes in common with the rest of the soft tissues of the entire body.

Prognosis is good for recent cases, provided proper treatment is carried out. It is bad for patients over fifty, for long-standing cases, for careless and injudicious patients, and for those who cannot or will not take a purely milk diet.

Treatment.—*Importance of early and thorough treatment.*—If treatment be undertaken sufficiently early in sprue, and be thoroughly and intelligently carried out, it is generally marvellously successful.

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Should, however, it be undertaken at too late a period, when the glands and the absorbing surface of the alimentary canal have been hopelessly destroyed, do what we will, the case is sure to end fatally. In prescribing a treatment, therefore, the first thing for the physician to do is to get his patient thoroughly convinced of the deadly nature of his complaint; for, unless he receives the hearty and complete co-operation of his patient, the physician must not expect to cure a well-established case. To be successful, treatment must be thorough, sustained, and prolonged. All predisposing causes, as uterine or other discharges, syphilis, scurvy, and the like, must of course be dealt with and, so far as possible, removed.

The milk cure.—By far the most successful treatment is what is known as the "milk cure." In carrying this out it is well to commence with a dose of some aperient—castor oil or pulvis rhei composita. Pending the action of the drug, all food, including milk, should be withheld. The patient should be sent to bed in order to economise strength and maintain an equable warm temperature of the skin. He should also be directed to clothe warmly, to encircle the abdomen with a broad flannel binder, to cover his arms and shoulders with a warm jacket, and to live in a large, sunny, warm room. When the purgative has acted the milk is begun. At first sixty ounces at most are allowed in the twenty-four hours, small quantities being given every hour or every two hours. When the patient is very weak the feeding must be continued during the night. *The milk should not be drunk, but sipped with a teaspoon, or taken through a straw or fine glass tube, or from a child's feeding bottle.* As a rule, on this regimen, in the course of two or three days, the patient's condition is very much improved. The stools have increased in consistency — are solid perhaps, the distension of the abdomen has subsided, dyspeptic symptoms have vanished, and the mouth is much less tender and less inflamed. The quantity of milk should now be increased at the rate of half a pint a day or every

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second day, until 100 ounces, or thereabouts, are taken in the twenty-four hours. It is well to keep at this quantity for ten days at least, when, everything going well, a gradual increase to six or seven pints may be sanctioned. Up to this point the patient should keep in bed; but when he has reached this quantity he may get up and, if he feels strong enough and the weather is mild, go out of doors. *For six weeks, dating from the time the stools become solid and the mouth free from irritation, no other food or drink whatever should be permitted.* A raw egg, if it is found to agree, may now be added to the milk; later, some artificial malted food; next, small quantities of well-boiled arrowroot, rusks, pulled bread, thin bread (stale) and butter, or other digestible form of starchy food; later still, chicken broth, a little fruit; and, by-and-by, fish and chicken may be gradually introduced.

Importance of prompt treatment of threatened relapses.—Should, however, the slightest sign of dyspepsia or flatulence, especially of diarrhœa, or of sore mouth show itself, then the extra food must be discontinued immediately, a dose of compound rhubarb powder administered, and the patient be sent back to bed and placed once more at absolute rest and on a pure milk diet. In convalescents, no matter how long the acute symptoms have been in abeyance, this prompt recognition and treatment of threatened relapse should be rigorously observed. This is a rule of the utmost value and importance. Procrastination in treatment, under these conditions, is exceedingly dangerous. Promptitude in recognising and treating relapse not only saves time, but it may avert hopeless intestinal atrophy.

Symptoms persisting.—In commencing this treatment, if the patient after two or three days be found unable to digest and assimilate so much as three pints of milk in the twenty-four hours, the daily allowance must be reduced by half a pint a day until thirty ounces or thereabouts only are taken. If now the motions become solid, the quantity of milk must be gradually increased by five or ten

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ounces a day, so that in the course of a few weeks the full allowance—six or seven pints—is consumed.

How to meet inadequate assimilation.—It sometimes happens that the quantity of milk can be raised to seventy or eighty ounces per diem, but no higher, further increase bringing on sore mouth, distension, and diarrhœa. In some of these cases the difficulty appears to depend not so much on digestion as on inability to absorb a large quantity of fluid. Occasionally, in such cases, one may succeed in getting the necessary amount of nutriment introduced by thickening the milk with condensed milk; or by slowly evaporating fresh cows' milk so as to reduce its bulk without diminishing the solids (Thin). The evaporation is best done in a vessel like a glue-pot, in which the milk is not boiled, but is surrounded by a jacket of boiling water; the milk during the process must be constantly stirred to prevent the formation of a scum. Or the milk diet may be supplemented by an adequate allowance of raw or underdone meat.

Other forms of giving milk.—Digestion is sometimes aided by peptonising the milk; or by mixing it with lime water or a little salt; or by aërating it in a soda-water syphon. Koumiss sometimes agrees for a time when ordinary milk fails, and, if necessary, should be tried. Similarly, white wine whey is occasionally digested when milk is not; it is often of great service, especially when an alcoholic stimulant is indicated.

Fruit treatment.—The value of fruit in the treatment of sprue and other forms of intestinal disease has long been recognised by a limited number of practitioners, particularly abroad. It is only lately that it has obtained any hold on medical opinion in England. I have long been in the habit of prescribing bananas and apples, tentatively of course, in these cases, and often with marked success. Of late repeated trials of the strawberry in sprue have confirmed me in my belief in the value of the fruit treatment, and in the strawberry treatment in particular. The plan I follow is to give one or two

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strawberries with each feed of milk, and, if found to agree, to increase the number gradually until two or three pounds are taken daily. Preserved fruits, particularly peaches and pears, make suitable substitutes if strawberries or bananas are not obtainable.

Treatment with meat juice and underdone meat.—Occasionally, symptoms persist or become aggravated under this system of treatment, and one is forced to conclude that milk does not suit the patient. In such cases raw meat juice will often prove an efficient substitute. The juice of four or five pounds of fresh lean meat, and a little water to allay thirst, may be taken in small quantities at short intervals daily. After a time, when the stools are reduced in number and quantity, although perhaps not quite solid, scraped meat, or very much underdone meat, and by-and-by a little charred toast, a plain rusk or biscuit, and so forth, may be gradually added to the diet.

Meat and warm water diet.—Not unfrequently, after the stools have become solid under a carefully regulated pure milk diet, it is found that any attempt to return to ordinary food, or to take anything beyond the most simple farinaceous dishes, is quickly followed by a recurrence of diarrhœa and the familiar flatulent dyspepsia. Such cases are sometimes successfully treated by a complete abandonment of milk, fruit, and farinaceous stuffs for a time, and placing the patient on what is known as the "Salisbury cure." This is a diet consisting only of meat and warm water. Commencing with smaller quantities, in time the allowance of meat is gradually raised to about three pounds *per diem*, taken at equidistant intervals in three or four meals. The meat must be of good quality, free from fat, coarse fibre, and gristle; it may be prepared as mince, or in the form of steak or chop, not too much cooked. Warm water, amounting in all to four pints in the twenty-four hours, is drunk before going to bed and on rising in the morning, and also about two hours before meals —never at meals. This course must be persisted in for six weeks, when ordinary food will be gradually

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attempted again. I have sometimes found it useful in cases of relapsing sprue to make the patient fast systematically one day a week, feeding him on that day on milk only. Sometimes, in cases of active sprue, I have found benefit by intermitting the pure milk diet for a day or two every week, and on these days feeding them on minced meat and hot water only.

Nutrient enemata or suppositories.—In all grave cases of sprue nutrient enemata or suppositories should be steadily administered every four or six hours. If tolerated they are most valuable aids to nutrition. It is well, when using them, to wash out the rectum once a day with cold water.

These methods of treatment—followed by a carefully-selected and increasing mixed diet, combined with warmth and rest—are in my experience the most successful methods of treating sprue; should they fail, the chances of recovery are poor indeed. Nevertheless, I have seen cases in which, after failure of the most carefully carried out milk or meat diets, a mixed diet proved successful for a time. In such mixed diets, in fact in all diets in sprue, *restriction in the amount* is as important, perhaps, as the quality of the food consumed. Food should never be given unless the patient is hungry. It is a great mistake to try to make these patients fat rapidly, or to stimulate the desire for food by encouraging active exercise. The bowel is not in a condition to deal with large meals.

When to send the patient to Europe.—When sprue develops in the tropics, if feasible the patient should be sent to Europe as soon as possible. It is a mistake, however, to ship an invalid with his disease active on him, or if his end is manifestly not very far off. Diarrhœa should not be active when the patient is put on board ship. In every case provision, such as a cow or an abundant supply of sterilised milk, should be made for carrying on treatment during the voyage.

The clothing and general management.—Sprue patients returning to Europe ought to be especially

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careful in their clothing, and they ought to get out their warm clothes before the ship leaves the tropics. If their return is during the winter, they should arrange to remain in the South of Europe till at least late spring. Next to an unsuitable dietary, perhaps cold is the most prejudicial influence to which a sprue case can be exposed. A sprue patient ought never to feel cold; he ought always to wear thick flannels, thick stockings, and, when up and about, thick boots. In winter a chamois-leather waistcoat, provided with sleeves, is of great service. His rooms ought to be warm. He ought to eat very sparingly. He ought never to be fatigued; he ought to go to bed early and rise late; in fact, he ought to do everything in his power to avoid irritating the bowel, to guard against chill, physiological depression, and the necessity for copious eating. During the summer England is suitable enough as a residence; but during the cold winter and spring months some milder, drier and more sunny climate must be sought out.

Drugs in sprue.—Experience soon teaches one to distrust medicines in sprue. Occasionally a gentle aperient or, if diarrhœa is watery and excessive, a few drops of laudanum are of service; but active drugging of all sorts is, as a rule, in the highest degree prejudicial. If the mouth is very painful, cocaine—five grains to the ounce—brushed on before eating will deaden sensibility and, for a time at all events, relieve suffering. Constipation must be carefully avoided, and a simple enema used if necessary.

I think it right to state that two methods of drug treatment seem, in some cases, to have been followed by good results. One, advocated by Dr. Begg, lately of Hankow, consists in the administration of repeated doses of yellow santonin. He recommends one or two doses of castor oil to commence with, and, thereafter, five grains of santonin in a teaspoonful of olive oil once or twice a day for a week, diet being at the same time attended to. The other method has gained for an irregular practitioner in Shanghai some

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reputation. It consists in the repeated administration of purgatives alternately with or before the exhibition of large quantities—two teaspoonfuls at a time—of some form of carbonate of lime, believed to be powdered cuttlefish bone or powdered crabs' eyes. I have tried the santonin treatment without benefit to patients. I have also used cuttlefish bone; in one case with the result of permanently stopping the diarrhœa but not of arresting the progress of the disease. In this case, although diarrhœa was most effectively checked, yet massive solid stools continued to pass. After a few weeks the patient died from asthenia, notwithstanding a liberal diet which, apparently, was digested but not absorbed.

Of late I have been in the habit of using intramuscular injections of very minute doses of arseniate of iron. In some instances the benefit from these injections has been prompt and marked. I would recommend their employment in every case of sprue in which anæmia is pronounced.

The sprue patient, if possible, ought not to return to the tropics. If compelled by circumstances to do so, he must exercise the utmost care with regard to his health, and avoid exposure, fatigue, cold bath, alcohol, and all excesses; take a minimum of, or avoid altogether, red meat; purge gently, and go on absolute milk diet on the slightest sign of relapse.

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CHAPTER XXXI

TROPICAL LIVER

THE subject of liver disease is everywhere a difficult and complicated one. It is especially difficult in tropical countries; for not only is the resident there liable to all the forms found in temperate climates, but he is exposed, in addition, to various potent predisposing and exciting causes of liver disease not present, or only present in a very mild degree, in more temperate latitudes. These additional causes of liver disease, inseparable from the tropics, are heat, malaria and, especially, dysentery. To these, too often, have to be added injudicious personal habits, a tendency to over-full and over-rich feeding, to over-stimulation by alcohol, and deficiency of muscular exercise.

The young European who finds himself in the tropics for the first time is surrounded very often by luxuries in the shape of food, wine, carriages, servants—luxuries to which he had not been accustomed perhaps in his home. At first the change, the excitement of novelty, and the high temperature act as stimulants to appetite, and the excessive loss of fluid by cutaneous transpiration creates a powerful thirst. Little wonder, therefore, that in such circumstances the youth, having the appetite and the opportunity of gratifying it, is apt to indulge in food and drink beyond safe physiological limits. He is made lazy by the heat; he cannot exercise during the day, and when evening comes he prefers lounging on the verandah or hanging about the club bar to walking or riding or games. Very likely he sits up late at night, drinking and smoking, so that in the morning he is too sleepy to ride out or take any other form of exercise. And so it comes about, what with a surcharge of aliment and alcohol, and the diminished activity of lung metab-

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olism and excretion incident to high temperature and muscular inactivity, that a very large and unusual amount of physiological work is thrown on the liver. With this large amount of work there is a corresponding hyperæmia. This may be considered the first stage of tropical liver—hyperæmia from functional activity; up to this point it is a purely physiological condition.

Pushed a step farther this physiological hyperæmia passes into congestion with blood stasis and consequent diminished functional activity. Hyperæmia of a physiological character will be evidenced by increase of functional activity, and there will be a copious flow of bile, sometimes causing diarrhœa of a bilious character, particularly morning diarrhœa. But when the limits of physiological hyperæmia are passed, and congestion of a pathological character sets in, the consequent arrest of function will be evidenced by pale stools, perhaps diarrhœa of a pale, watery, frothy, fermenting character—in the last case the diarrhœa doubtless depending, in part at least, on fermentative processes set up in the contents of an alimentary canal no longer kept relatively aseptic by an adequate supply of healthy bile. Other symptoms of this condition are headache, furred tongue, scanty, high-coloured, loaded urine, a feeling of weight or fulness, or even of pain in the region of the liver, and, probably, enlargement of the percussion area and other physical signs of enlargement of that organ. One step farther and such a condition may pass into actual hepatitis attended with fever, smart pain in the liver, tenderness on percussion, and still more marked increase of the hepatic area.

A functionally very active hyperæmic organ is prone to inflammation, even on slight cause. In the case of the hyperæmic liver a common cause of inflammation is chill, such as may arise from a cold bath, a wetting, or from lying uncovered on a warm night in a current of air. The experienced resident knows this very well, and is at great pains to guard against such an occurrence. He very likely wears what is known as a cholera belt; he sleeps, even on the warmest night,

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in flannel pyjamas, and with a thin blanket drawn over his abdomen; during the day he wears a woollen undervest and very likely serge or thin tweed clothes. He does not sit down in damp clothes, and he has a great respect for a shower of rain. Besides chill, there are other causes which may convert the hyperæmia into congestion or inflammation; a blow may operate in the same way, so may a surfeit of eating or drinking, so may exposure to the sun, so may an attack of malarial fever or of dysentery.

Treatment.—Nature sometimes effects a cure in these cases of hepatic congestion by establishing a smart diarrhœa. In the treatment of such cases we cannot do better than to imitate Nature, and even to supplement her efforts. A few doses of the sulphates, in the shape of some kind of bitter water or of Carlsbad salts, generally give prompt relief. But if the subject of such attacks does not profit by experience and mend his ways, very likely his liver, in time, will become chronically hyperæmic and extremely liable to intercurrent attacks of congestion of a character more or less acute. The subjects of this type of "liver" ought to be most careful in their habits. They must not lie abed too long; they must not take cold baths; they must not take cold drinks, nor expose themselves to cold in any form; they must clothe warmly; and they must eschew alcohol in every shape. Animal food they must partake of but sparingly; and they should give the preference to fowl and fish over beef and mutton. Fruit and farinaceous food may be more freely partaken of, but over-eating in every form must be avoided. Exercise should be taken at least twice a day; and, at least once in twenty-four hours, the exercise should be of such a character as to provoke perspiration. A gallop on horseback, a smart game of tennis or rackets, are excellent hepatic stimulants. Occasionally, once a week or not so often, particularly when a sense of fulness or aching in the right side seems to indicate that all is not right with the liver, a dose of Carlsbad salts or bitter water, preceded perhaps by a few grains of calomel, may avert more serious trouble.

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When hyperæmia becomes chronic, when the patient is continually suffering with "liver," he should leave the tropics for a time. Nothing relieves these cases of chronic congestion so quickly or so effectively as a visit to Carlsbad or to Harrogate, and a thorough course of the waters there and of the dietetic restrictions imposed in the Carlsbad cure. This should be followed up by country life in England and the active pursuit of country sports; the usual precautions in the shape of warm clothing, avoidance of cold baths, chills, alcohol, and high living being scrupulously observed and a weekly saline purge taken.

A serviceable imitation of the natural Carlsbad water may be made by dissolving fifty-three grains of the powdered salt in a pint of boiling water.* This may be divided into three equal portions, which are to be sipped as hot as possible, at intervals of twenty minutes, on an empty stomach, first thing in the morning. While taking the solution gentle exercise, as moving about the room, should be indulged in. Breakfast must not be taken till an hour after the last dose. If the bowels are not gently acted on, an increased quantity of the salts should be taken. During the course, which should be persevered in for three weeks, the diet must be carefully regulated; butter, fat, nuts, fruits, pastry, preserves, tinned foods, cheese, salads, wines, spirits, and beer are to be avoided. Too much meat must not be taken; a small meat meal once a day must suffice. The quantity of food, too, should be restricted, and clothing, exercise, and bathing be carefully attended to. Much excellent advice on the subject of the Carlsbad treatment will be found in Surgeon-Major Young's book, "The Carlsbad Treatment for Tropical Ailments," published by Thacker, Spink & Co., Calcutta.

During severe attacks of acute congestion, or of severe hepatitis attended with fever and much local distress, the patient must be kept in bed and placed on a very low diet of thin broths, barley water, or

* A good substitute for Carlsbad salts consists of sod. sulph. 2 parts, sod. bicarb. 1 part, sod. chlorid. 1 part.

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rice water, or milk and water. He should be purged freely and often with salines. A large hot poultice, two feet or more in length by one foot in breadth, should be laid over the region of the liver; such a poultice to be effective should pass from the centre of the back to well over the epigastrium. Dry cupping sometimes gives marked relief. Muriate of ammonia has a certain reputation in these cases; it should be prescribed in twenty-grain doses every six or eight hours. I have often used it, but I cannot vouch for its virtues; it does no harm.

When such a hepatitis is associated with dysentery, should it resist these milder measures thirty to sixty grains of ipecacuanha often give marked relief. This dose should be repeated every twelve or twenty-four hours for two or three times. When the hepatitis is associated with malarial fever, full doses of quinine, in addition to the purging and the other measures already mentioned, are indicated.

Whether hepatitis, unless associated with dysentery, ever passes on to suppuration is a moot point. Some say that it may; others resolutely deny that there is such a thing as "tropical abscess" unassociated with dysentery. This subject will be discussed in the following chapter. Malarial hepatitis has already been considered (p. 95).

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CHAPTER XXXII

ABSCESS OF THE LIVER

Definition.—A form of suppuration in the liver, occurring especially in warm climates, principally in male Europeans and in association with dysentery.

Geographical distribution.—Abscess of the liver, of the type known as tropical abscess, is, for the most part, a disease of warm climates. Usually a sequel, or, it may be, a concomitant of dysentery, it is rare or altogether absent in countries where dysentery is also rare or absent. Its geographical distribution, therefore, is in the main regulated by that of dysentery. It has to be noted, however, that liver abscess is not a sequel or concomitant of the dysentery of all countries and at all times. Thus it is rare as an indigenous disease in temperate climates, even in those temperate climates in which dysentery is at times common enough. Again, in tropical climates the dysentery and liver abscess curves do not everywhere and at all times maintain a constant and definite relation to each other; for, even in hot countries, the dysentery of some places is more apt to be followed by liver abscess than is the dysentery of other places; and, even as regards dysentery in the same place, some epidemics are more apt to be associated with liver abscess than are others. Nevertheless, on the whole, it may be laid down as a fairly general law that in the tropics and sub-tropics the liver abscess curve follows, in the main, the dysentery curve; and that the geographical range of liver abscess in these climates is the same as that of dysentery.

In Great Britain the liver abscesses met with occur most frequently in individuals who manifestly had contracted the disease in the tropics. As a disease of indigenous origin, notwithstanding the considerable amount of dysentery in lunatic

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asylums and similar large public institutions in Great Britain, it is distinctly rare, though not so uncommon as is usually supposed. Of course this remark does not apply to those suppurations which are connected with ordinary pyæmia, with gall-stones, hydatids, pylephlebitis, and the like; it applies only to dysenteric and, possibly, if there be such a disease, to idiopathic abscess. In northern and central Europe it is much the same in this respect as in Britain. The disease is more frequent in southern Europe—in Italy, Greece, the Balkan peninsula, and south Russia; it is said to be particularly common in Roumania. In eastern Asia, even outside the tropical belt, it is far from rare: thus it is not uncommon in Japan, and it is a very notable feature in the morbidity of Shanghai and the coast of south China. In North and Tropical Africa it is common enough; indeed, some of the best modern studies of the disease have been made in Egypt and in the Algerian province of Oran. In the western hemisphere there is a corresponding distribution; fairly common in the tropics, it becomes progressively rarer as we proceed north and south. It is apparently less common in the West Indies than in India and the East generally. In the southern hemisphere, although the Cape and Transvaal and the cooler parts of Australia seem to enjoy a practical immunity, the European in the Northern Territory of Australia and in the neighbouring island of New Caledonia is subject to this disease.

The apparent caprice in the geographical distribution of liver abscess is probably, in great part, explained by what has already been stated with regard to the distribution of amœbic dysentery, and to the effects of high atmospheric temperature and tropical habits on the European liver, together with the circumstance, as will be mentioned in the sequel, that the amœba is an important, if not a principal, element in the production of tropical liver abscess Evidence tends to show that liver abscess is the sequel or *associate of amœbic dysentery*—a disease practically confined to warm climates; not of bacillary

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dysentery, the only form of dysentery occurring in temperate and some warm climates.

Ætiology.—*Relation to dysentery.*—There can be no question as to the existence of an intimate relationship between dysentery and liver abscess. Numerous and well-authenticated statistics, as well as everyday experience, attest this. In 3,680 dysentery autopsies made in various tropical countries, and collated by Woodward, 779 (21 per cent.) revealed abscesses of the liver. To quote recent Indian experience:—According to the Annual Report of the Sanitary Commissioner with the Government of India for 1894, out of 465 European soldiers who died from dysentery in India during the period 1888–94, 161 (35 per cent.) had, in addition to dysenteric lesions, abscess of the liver. Conversely, in Egypt, Kartulis, in an experience of over 500 cases of liver abscess, elicited a history of dysentery in from 55 to 60 per cent.; Zancarol, also in Egypt, in 444 cases, elicited a similar history in 59 per cent.; and Edwards and Waterman, in 699 collated cases, elicited a like history in 72·1 per cent. During the period 1870–95, of 45 cases of liver abscess treated at the Seamen's Hospital, Greenwich, and collated by Mr. Johnson Smith, *post-mortem* evidence or a distinct history of dysentery was obtained in 38 (84·4 per cent.).

These figures are conclusive as to the existence of an intimate relationship between dysentery and liver abscess. There is good reason, however, for believing that, while they represent the truth, they do not represent the whole truth, and that the association is even more frequent than they indicate. As has been pointed out by Macleod and others, the occurrence of antecedent dysentery in cases of liver abscess is very often overlooked; for, without a *post-mortem* examination, it may be impossible to pronounce definitely on this point in every instance. It is also well known that extensive dysenteric ulceration may be present and yet give rise to no active subjective symptoms whatever. Moreover, many patients suffering from liver abscess forget, or fail to mention, the occurrence of a previous dysenteric

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attack, or may mislead the physician by describing such an attack as "diarrhœa." Further, at *post-mortem* examinations, dysenteric lesions of a superficial and apparently trifling character are often either not sought for, or are overlooked, or have disappeared. Consequently, although the evidence of antecedent dysentery may not be forthcoming in a proportion of cases of liver abscess, it must not be concluded that in these cases there has been no dysentery.

In a masterly paper Macleod, after a very careful and critical analysis of certain figures bearing on this subject, concludes that dysentery is a factor in nearly every case of tropical liver abscess. In forty cases of the disease observed in Shanghai he had positive evidence of dysentery in all except one; and even in this case, as recovery ensued, there was no certainty that dysenteric lesions had not been present. Perhaps Macleod's conclusions are somewhat too sweeping; I confess, however, that they are, in the main, in harmony with my own experience. Doubtless they apply to liver abscess as met with in Shanghai and, probably, in many other places. It is just possible, however, that what holds good for one place may not hold good for all places, and that Bombay, for example, may differ in this respect from Shanghai. In the Sanitary Commissioner's Report, above referred to, it is stated that in 2 (3 per cent.) instances only, out of 74 cases of liver abscess occurring in the Bombay Presidency in the period 1888–94, were there dysenteric associations. It is difficult to believe that, did it always exist, so important and evident a circumstance as dysentery had been overlooked in 72 out of 74 cases. It is equally difficult to believe that the liver abscess of Bombay is associated with dysentery in only 3 per cent. of cases, whilst, according to the same authority, in the whole of India it is certainly so associated in at least 30 per cent. of the total cases. Manifestly, the statistical aspect of this important question requires re-study in the light of more careful clinical and *post-mortem* observation.

Another important point, yet to be definitely

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settled, is the exact relationship in point of time of the dysentery to the liver abscess. In the great majority of cases the dysentery antedates the abscess. But many clinicians have held that in some instances the relationship is reversed; that in others the two diseases are from the commencement concurrent; whilst in others, again, hepatitis, presumably of a kind which may eventuate in abscess, alternates with active dysenteric symptoms. If the abscess antedate the dysentery, then the dysentery cannot be the cause of the abscess. On these grounds some pathologists have regarded liver abscess and dysentery as but different expressions of one morbid condition; reacting to some extent on each other, but not directly related the one to the other as cause and effect. Here, again, the latency as regards symptoms of some dysenteries has to be discounted in attempting to settle the question on clinical grounds only.

Race and sex.—Besides this matter of its relationship to dysentery, there are several well-ascertained facts to be reckoned with before we can arrive at sound views on the subject of the ætiology of liver abscess.

(1) Though common in Europeans in the tropics, liver abscess is rare among the natives. Thus, in the native army of India the proportion of deaths from liver abscess to the total mortality in 1894 was only 0·6 per cent., whereas in the European army it was 7·4 per cent. Man for man, the relative liability of the European soldier and the native soldier was as 95·2 to 4·8.

(2) This disproportion is in spite of the fact that the native is more liable to dysentery than the European. Thus, in 1894, in the Indian army the admission rate among the native troops for dysentery was 43·8 per thousand, whereas in the European troops it was only 28·6; and in every hundred deaths in the native army 4·7 were from dysentery, against only 3·8 in the European army.*

* Dr. Rees informs me that liver abscess is more common among the natives of Nigeria than these figures seem to show it to be among the natives of India. Among the negroes, he says, the mortality in dysentery is much higher than among Europeans resident in Nigeria. Of those negroes attacked with dysentery who lived long enough, many subsequently developed liver abscess.

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(3) European women in the tropics, though quite as subject to dysentery as European men, rarely suffer from liver abscess; children hardly ever.

(4) The rarity of liver abscess in temperate climates.

Predisposing conditions.—The foregoing considerations seem to indicate that for the production of liver abscess at least two things are necessary—a predisposing cause, and an exciting cause. Dysentery is certainly not always and alone both the exciting and predisposing cause. Were this so, the native soldiers and the European women and children in India would suffer as frequently from liver abscess as do the European males there. Some additional factor evidently complicates the problem.

As liver abscess is developed principally in tropical climates and in European visitors there, and much more rarely in the native, it would seem that tropical conditions in those unaccustomed to them are in some way bound up with this predisposing element; and as liver abscess is rare in European women and children, it would seem that these conditions are in some way specially operative on European men. We have grounds, therefore, for concluding that, in addition to general tropical conditions, it must be the greater amount of exposure to which men, as compared with women and children, are subjected in the course of their business and amusements; or some other condition, especially that one which is relatively more common in men than in women and children, and which is a universally recognised cause of hepatic disturbance—over-indulgence in stimulating food and alcoholic drinks—that constitutes this predisposing cause. Intemperate habits and exposure, doubtless, lead to a special liability in men to a hyperæmia and congestion of the liver tissue by which its resistance to pathological influences is impaired. In these circumstances, pathological influences which in the healthier condition of the organ—such as we assume to exist more generally in natives and in European women and children—would have been successfully overcome,

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gain the upper hand and lead to suppurative disintegration of the organ. In support of this view we have the statement of Waring, that 65 per cent. of liver abscesses observed by him were in alcoholics; and it is also said that when the native takes to European habits in the matter of eating and, especially, of drinking, his liability to liver abscess is greatly and proportionately increased.

I conclude, therefore, that in the vast majority of instances the exciting cause of liver abscess is dysentery; the predisposing cause hyperæmic, congestive, or degenerative conditions incidental to tropical life, supplemented by such things as exposure and unphysiological habits in eating and drinking.

Supplementary causes.—It is conceivable that in a highly predisposed liver exciting causes other than dysentery, such as a blow or sudden aggravation of chronic congestion by chill or excess, may suffice at times to determine suppuration. Liver abscess is most prone to develop at the commencement of the cold season. Further, one can conceive that in a hyperæmic liver struggling to resist dysenteric suppurative influences some third condition, such as the blow, chill, or surfeit referred to, may contribute to or determine the formation of abscess which, in their absence, might have been averted.

Briefly stated, the causes of liver abscess are, first, predisposing—hyperæmic and degenerative conditions of the liver; second, exciting—dysentery, or dysentery combined with chill, dietetic excess, or traumatism.

Influence of age and length of residence.—Liver abscess may occur at any age after childhood, but is most common between twenty and forty. It is most prone to show itself during the earlier years of residence in the tropics (40 per cent. in the first three years), although the older resident is by no means exempt.

Influence of malaria.—Malaria, by causing frequent attacks of hepatic congestion and by lowering the general vitality, may have some predisposing influence; but, as already pointed out, malarial hepatitis is essentially of a plastic and not of a suppurative nature. It is a common mistake to suppose that

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malaria causes the suppurative liver disease of the tropics; the two concur geographically to a certain extent, but are in no way ætiologically identical.

Morbid anatomy.—It may be inferred from the symptoms that in the early stages of suppurative hepatitis there is general congestion and enlargement of the liver; in some instances this condition may be more or less confined to one lobe or even part of a lobe. Later, as we know more especially from observations in cases that have died from the attendant dysentery, one or more greyish, ill-defined, anæmic, circular patches, half to one inch or thereabouts in diameter, in which the lobular structure of the gland cannot be made out, are formed. These grey spots are very evident on section of the organ. A drop or two of a reddish, gummy pus may be expressed from the necrotic patches—for such they are. Still later, the centres of the patches liquefy, and distinct but ragged abscess cavities are formed. An abscess thus commenced extends partly by molecular breaking down; partly by more massive necrosis of portions of its wall; partly by the formation of additional foci of softening in the neighbourhood and subsequent breaking down of the intervening septa. The walls of such an abscess have a ragged and rotten appearance. Spherical on the whole, there may be one or more diverticula extending from the main cavity; or contiguous abscesses may break into each other and communicate by a sinus. Occasionally a thickened blood-vessel is met with stretching across the cavity. Though the pus and detritus lying on the abscess wall are viscid and adhesive, there is no notable exudation of lymph either lining the cavity or in the still living liver tissue beyond. There is a peripheral zone of hyperæmia; beyond this zone the gland may appear normal or simply congested.

Number, size, and situation of abscesses.—Liver abscess may be single or multiple. If multiple, there may be two, three, or many abscesses. Zancarol's statistics, applying to 562 cases, give the proportion of single to multiple abscess cases as three of the former to two of the latter.

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When single the abscess sometimes attains a great size. Frequently it is as large as a cocoanut or even larger; it has happened that the entire liver, with the exception of a narrow zone of hepatic tissue, has been converted into a huge abscess sac. When multiple the individual abscesses are generally smaller, ranging in size from a filbert to an orange.

As might be expected from considerations of the relative size of the parts, abscess is much more common in the right than in the left and smaller lobes. What might be termed the seat of election is the upper part of the right lobe. Roux gives the proportions in 639 cases as 70·85 per cent. right lobe, 3 per cent. left lobe, and 0·3 per cent. lobus spigelii.

Adhesions to surrounding organs are frequently, though not invariably, formed as the abscess approaches the surface of the liver. In this way the danger of intraperitoneal extravasation is usually averted.

Pulmonary inflammation and abscess from escape of liver pus into the lungs are sometimes discovered *post mortem*. Generally the pulmonary abscess communicates with the mother abscess in the liver by a small opening in the diaphragm.

Liver pus.—The naked eye appearance of liver pus is peculiar. When newly evacuated it is usually chocolate-coloured and streaked with, or mixed with, larger or smaller clots or streaks of blood, and here and there with streaks of a clear mucoid or yellowish material. It is so thick and viscid that it will hardly soak into the dressings; it lies on the surface of the gauze like treacle on bread, spreading out between the skin and the dressing, and finding its way past the edge of the latter rather than penetrating it. When quite fresh, here and there little islands of what may be described as laudable pus may be made out in the brown mass. Sometimes it contains considerable pieces of necrotic tissue. Occasionally, from admixture of bile, the abscess contents are green-tinged. Liver purulage has always a peculiar mawkish odour; it is rarely offensive, unless

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the abscess lie near the colon, in which case it may have a fæcal odour. Under the microscope many blood corpuscles are discoverable, besides much broken-down liver tissue, large granular pigmented spherical cells, leucocytes, *débris*, oil globules, hæmatoidin crystals, and, occasionally, Charcot-Leyden crystals and amœbæ; rarely the ordinary pyogenic bacteria.

Amœbæ and pyogenic organisms.—According to my experience of tropical abscess of the liver seen in England, amœbæ can be detected in considerably over half the cases. This agrees with Kartulis's experience in Egypt, and that of others elsewhere. Rogers concludes from a careful examination of scrapings from the walls of a large number of liver abscesses in Calcutta, that the amœba is always present. I have observed in a good many instances in which I have failed to detect the amœba in the aspirated liver pus, or in the pus which escaped at the time of operation, that the parasite appeared, often in great profusion, four or five days later in the discharge from the drainage-tube. I have seen them in these circumstances in strings of eight or ten; the string-like arrangement suggesting that they had developed in some tube, such as a blood or bile vessel. The amœbæ persist in the discharge until the abscess has healed. It is justifiable to infer from the absence of amœbæ from the pus constituting what might be called the body of the abscess, and their appearance in the pus coming from the walls of the abscess a few days later, that the habitat of the parasite is not so much the pus occupying the general abscess cavity as that immediately in contact with the wall and the breaking-down tissues themselves. This is an inference entirely in harmony with Councilman and Lafleur's demonstration, confirmed by Marshall, of the parasite in the still living tissues around the abscess. In my experience the presence of the amœba does not affect prognosis unfavourably. Lafleur says it does: I cannot agree with him. In common with many other observers I have often seen amœbic liver abscess recover completely and rapidly after operation.

Other protozoa have been found in liver pus.

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Thus, both Grimm and Berndt have found numerous active flagella-like organisms therein. Some time ago, in the expectorated pus from a liver abscess discharging through the right lung, I found a ciliated infusorian resembling *Balantidium coli.*

In the pus of a large proportion of liver abscesses, both microscopic examination and culture may fail to detect the usual pyogenic micro-organisms. To harmonise this well-established fact with modern views on the cause and nature of the suppurative process, it has been suggested that, though in these sterile abscesses micro-organisms had originally been present, they had subsequently died out. This view receives a measure of support from the fact that in a proportion of instances there is no difficulty in demonstrating in the pus the ordinary pyogenic bacteria and, sometimes, the *Bacterium coli commune.* It by no means follows from this circumstance, however, that bacteria are a necessary factor in the production of all liver abscesses.

Encystment.—In rare instances the pus of liver abscess, instead of possessing the chocolate colour and viscid consistency described above, is yellow and creamy. This is particularly the case when the abscess becomes encysted—an occasional event. The walls of these encysted abscesses are thick, smooth, resistant, and fibrous. In time their contents become cheesy, and ultimately cretified; in the latter event the cyst shrivels up and contracts to a small size.

Pathology.—The pathology of liver abscess has been a fruitful source of speculation and controversy. Much confusion has crept into the question from attempts to separate, ætiologically and pathologically, multiple from single liver abscess. The former is often called "pyæmic abscess" or "dysenteric abscess," and has been set down as being the peculiar sequel of dysentery; the latter has been called and considered the "tropical abscess" *par excellence*, and regarded as idiopathic and entirely unconnected with dysentery.

As already pointed out, a careful examination of

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cases and statistics shows that both forms of abscess, single and multiple alike, are, in the vast majority of instances, clearly associated with dysentery. In their respective clinical histories, in their symptoms, in the characters of their walls and contents, in the frequent presence of amœbæ, single and multiple abscesses are practically identical. The only difference between them is a numerical one—a circumstance quite inadequate to base a doctrine of specific distinction upon.

The view which I incline to hold on this subject has already been partly indicated in the section on ætiology. There are two factors which are principally concerned in the production of liver abscess: (1) the predisposing—weakening of the resistive faculty of the liver by chronic congestion or tissue degeneration, and, perhaps, other subtle changes brought about by a combination of climatic, dietetic, and other tropical conditions; (2) the exciting—some micro-organism, streptococcus, staphylococcus, *Bacterium coli commune*, amœba, or other parasite which, coming from the ulcerated dysenteric colon, or by way of the portal circulation (Marshall has recently demonstrated *Amœba coli* in a thrombus in a branch of this vessel), gains access to the liver and proliferates in the weakened tissues. In at least 90 per cent. of cases the micro-organism is associated with or derived from dysenteric processes in the colon. Whether the resulting abscess be single or multiple is more or less a matter of accident. If the weakened liver is efficiently inoculated at one point only, there is only one abscess; if at many points, then there is multiple abscess. This is virtually, in a sense, Budd's theory expressed in modern terms.

An apparently weighty objection to this view is sometimes urged. Why, it is asked, if liver abscess be the result of septic absorption from a dysenteric ulcer, is it not a common sequel of typhoidal or of tuberculous ulceration in the tropics? Macleod has met this objection very ingeniously and, I believe to a certain extent, correctly. He points to the fact

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that typhoidal and tuberculous ulcerations are surface lesions unattended with abscess formation in the wall of the bowel. In their case there is free escape of the products and germs of ulceration; whereas in dysenteric lesions, in addition to the superficial ulceration, there is often what is really abscess formation with burrowing and retention of pus below the mucous membrane, and therefore great liability to entrance of micro-organisms into the radicles of the portal vein. Liver abscess, therefore, according to this view, is a pyæmic process. Often, however, it must be confessed, the dysentery preceding liver abscess appears, judging from the symptoms, to be of the catarrhal rather than of a more severe type; but even in this case it may be that the amœba penetrates the portal radicle without producing ulceration.

To what extent the amœba is concerned in the production of tropical liver abscess it is as yet impossible to state. If the frequency of its presence is any indication it must be the usual if not the only cause. If we watch the movements of this animal on the warm stage; and if we reflect that it lives and wanders about in the same very active way among the structures forming the walls of the liver abscess, and even in what are comparatively sound tissues, preceding, as it were, the suppuration; and consider that it lives at the expense of these tissues, it is hard to resist the conclusion that the amœba must operate as a disintegrating and irritating agency. Kartulis suggests that it may act merely as a carrier of pus-forming bacteria. Others maintain that it is a harmless epiphenomenon, incapable in any way of inducing pus-formation. As yet experimental pathology has not given a decisive answer to this, one of the most important questions in tropical pathology.

Calmette, in view of the frequency with which he and others have found liver abscess to be sterile, suggests that the exciting agency is of a chemical nature, some irritating liquefying body derived from the decomposition processes going on on the surface of the dysenteric ulcer.

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Symptoms.—There is great variety in the grouping of symptoms in liver abscess. The following is a common history.

The patient, after residing for some time in the tropics, during which he enjoyed good general health and lived freely, was attacked by dysentery. In due course he appeared to recover, and resumed work. Several weeks or months elapsed when, after a wetting, or some such incident, he began to feel out of sorts, to suffer from headache, foul tongue, want of appetite, irregularity of the bowels, disturbed nights, excessive and unaccountable languor, irritability of temper, and depression of spirits. About the same time he began to be conscious of a sense of weight and fulness in the right hypochondrium. Later, he became feverish, particularly towards evening, the oncoming of the febrile distress being sometimes preceded by a sense of chilliness. At times he had sharp stabbing pain in the right side in the region of the liver, perhaps a dry cough and, possibly, a gnawing, uncomfortable sensation or pain in the right shoulder. His friends observed that his face had become muddy and haggard. He was uneasy if he lay on his left side. The quotidian rise of temperature now became a regular feature, the thermometer every evening touching 102°—sometimes more, sometimes less—and sinking to near normal by morning. He now began to perspire profusely at night, and even during the day when he chanced to fall asleep. He had to change his sleeping clothes once or even twice every night on account of the drenching sweats.

On examination it is found that the patient is somewhat emaciated; his complexion thick and muddy; his pulse 80 to 100; his tongue furred and yellowish; the palms of his hands and soles of his feet cold and clammy. As he lies on his back it is obvious, on inspection, that the epigastrium is too full for one so emaciated; and it is seen that the breathing is shallow and mainly thoracic. The right rectus muscle is rigid. Considerable discomfort, if not pain, is elicited by attempts at palpation and percussion over the right hypochondrium. The liver dulness extends an

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inch too high, and an inch or more beyond the costal border in the nipple line; posteriorly, it rises to about the eighth rib in the line of the angle of the scapula. It is further observed that the line of dulness is arched along its upper border; and that it is altered by changes of position, the upper line descending when the patient lies on his left side or stands up; in the latter position the lower margin descends markedly in the epigastrium. On deep inspiration, percussion below the right costal border gives rise to much uneasiness or even to acute pain. Very likely one or two tender spots can be discovered on firm pressure being made with the finger tips in some of the lower right intercostal spaces, or below the right costal margin. The spleen is not usually enlarged. Auscultation may detect pleuritic friction somewhere over the base of the right lung, or peritoneal friction over the liver itself. The urine, free from albumin, is scanty, high coloured, and deposits urates. The blood shows well-marked polymorphonuclear leucocytosis.

As the case progresses emaciation increases; hectic with drenching nocturnal sweats continues; the liver dulness and pain may further increase; or the general enlargement may somewhat subside, and percussion may reveal a pronounced local bulging, upwards or downwards. If the abscess which has now formed is not relieved by operation, after months of illness the patient may die worn out; or the abscess, which has attained enormous dimensions, may burst into the right lung or pleura, or elsewhere, and be discharged, and either recovery, or death from continued hectic and exhaustion or from some intercurrent complication, ensue.

The great variety in the urgency of symptoms.—Although the foregoing is a fairly common history in liver abscess, there are many instances in which the initial symptoms are much more urgent, and in which the disease progresses much more rapidly. In other instances subjective symptoms are almost entirely absent; or so subdued that the true nature of the case may be entirely misapprehended until the abscess bursts through the lung or bowel, or a fluctuating

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tumour appears in the neighbourhood of the liver; or, perhaps, not until after death, when the unsuspected abscess is discovered on the *post-mortem* table.

Fever.—In an acute sthenic case the initial inflammatory fever may run fairly high and persist for some time. Later, when it may be assumed that pus has formed, the fever becomes distinctly quotidian and intermittent in type, the morning temperatures being normal, or only slightly above normal, the evening rising to 101° or 102°, or a little over or under this. Sometimes evening temperatures of 103°, rarely of 104°, are registered. In the asthenic and insidious type, at first there may be short flashes of feverishness at more considerable intervals, to be followed later by a steadier fever of a hectic type, as in the suppurative stage of the sthenic cases. In either type there may be afebrile intervals of several days' duration; and in either there may also occur, concurrently with aggravations of the local conditions, spells of continued high temperature. Occasionally, though rarely, liver abscess may be unattended by fever of any description whatever.

Rigors.—In the classical descriptions of liver abscess the occurrence of violent rigor is generally mentioned as a notable sign of the formation of pus. Undoubtedly such a rigor does at times signalise this event; but it is by no means constant, and its absence is no guarantee that abscess has not formed. Generally the evening rise of temperature is preceded by a sense of chilliness, sometimes by a more marked rigor simulating, in the regularity of its recurrences and in its severity, the rigor of a quotidian malarial fever.

Sweating, particularly nocturnal sweating of a very profuse character, is an almost invariable accompaniment of liver abscess. The patient's clothes may be literally drenched with perspiration. Even during the day—particularly, as already mentioned, if he chance to fall asleep—the sweat may stand in beads upon the forehead and around the neck. This, like most of the other symptoms, may be temporarily absent or, in a small proportion of cases, trifling.

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The *complexion* is generally muddy, cachectic, and slightly icteric-looking; marked jaundice, however, is uncommon.

Wasting is generally decided and progressive.

Rheumatic-like pains and swelling of the hands and feet, such as occur in chronic septic affections, are sometimes to be noted. They usually disappear rapidly when the abscess bursts or is opened and free drainage is established.

Pain of some description is rarely absent. In a few exceptional cases there is no pain; such a patient may declare that he does not know that he has a liver.

There are several types of pain—local and sympathetic—associated with liver abscess. Complaint is almost invariably made of a sense of fulness and of a sense of weight in the region of the liver, not unfrequently referred to the infrascapular region. Stabbing, stitch-like pain, increased by pressure and especially by deep inspiration, by coughing and all sudden jarring movements, is very common, and probably indicates perihepatitis from proximity of the abscess to the surface of the organ. Percussion, or firm palpation, especially if practised during deep inspiration and below the ribs in front, generally causes smart pain and decided shrinking, the rectus muscle starting up as if to protect the subjacent inflamed parts. Pain on swallowing, at the moment the bolus of food traverses the lower end of the œsophagus, was mentioned to me by a medical man, himself the subject of hepatic abscess, as being a marked symptom in his own case. Pain on firm pressure with the finger tips in an intercostal space, and over a limited area, is a common and valuable localising sign. Among the sympathetic pains may be mentioned shooting pains radiating over the chest and down the right flank and hypochondrium.

Pain in the right shoulder.—This symptom is present in about one-sixth of the cases. It may be persistent, or it may intermit; it may radiate to the side of the neck, or to the region of the scapula, or down the arm; or it may be limited to the shoulder

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tip and clavicular region. In some instances it is of a dull, gnawing, aching character; in others it is more acute; and in some it may be represented by a burning sensation, as if the surface of the skin had been flayed by a blister. This symptom is a reflex transmitted from the hepatic terminals of the phrenic through the fourth cervical to the branches of the cervical and brachial plexuses.

Cough of a dry, hacking character, doubtless also a reflex from irritation of the diaphragm, or from an inflamed condition of lung or pleura over the seat of abscess, is not uncommon. When the abscess discharges through the lung, cough is sometimes very severe and may cause vomiting.

Respiration is generally shallow and proportionately rapid. This is partly symptomatic of the attendant fever; oftener it is owing to the fact that fuller inspiration is attended with stitch. Sometimes the breathing is entirely thoracic, the lower part of the chest seeming to be fixed—especially the right side—and the diaphragm almost motionless.

The *decubitus* is usually dorsal or right dorsal, the body being somewhat bent towards the right side and the right leg perhaps slightly drawn up. When the patient stands, a stoop to the right may be noticeable. Lying on the left side generally causes pain from dragging on adhesions, or discomfort from the pressure of the enlarged liver on the heart and stomach. Occasionally the decubitus is indifferent, or even on the left side.

The *digestive organs* are usually disturbed and the tongue is coated. Vomiting may occur from time to time, arising either from pressure on the stomach by the swollen liver or as an expression of gastric catarrh; appetite, as a rule, is poor; flatulence may be troublesome; the bowels are confined or irregular, or there may be diarrhœa or dysentery. In the case of concurrent dysentery, it may be noted sometimes that the hepatic and dysenteric symptoms alternate in severity.

The *area of hepatic percussion dulness* is usually extended upwards and downwards, and sometimes

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horizontally. The extension may be general, especially in the earlier stages; later, careful outlining of the upper and lower boundaries may discover a limited and dome-like increase in one direction, most significant if upwards. The upper line of dulness is not, as a rule, horizontal, as in hydrothorax; almost invariably, on approaching the spine, it trends downwards more markedly than in hydrothorax or empyema. Variations in the extent of the dulness may take place from time to time, and sometimes very rapidly, depending not on fluctuations in the size of the liver abscess, but on the varying and relative amounts of local and general hepatic congestion. One sometimes finds even a narrow hepatic dulness in the nipple line, with a great increase in the axillary or scapular lines. In one case the lower border of the liver may be as low as the umbilicus; in another, especially in front, it may be well inside the costal margin. Diagnosis in the latter type of case is difficult, and depends rather on the nature of the fever and on the history and general condition than on local signs.

Splenic enlargement may be present even when there is no malarial complication. This is rare, however, and in uncomplicated cases is seldom great. I have seen splenic tumour closely simulated by abscess in the left lobe of the liver.

Varicosity of the epigastric and hæmorrhoidal veins—one or both—is sometimes discoverable.

Œdema of the feet and ascites are rare in the earlier stages; but the former is very usual towards the termination of long-standing cases.

Local œdema over one or more intercostal spaces, or more extensive and involving the whole or part of the hepatic area, is sometimes apparent. When limited it is a useful locating symptom.

Local bulging, if attended with fluctuation, indicates the presence of pus near the surface and the pointing of the abscess. Usually this, when it occurs, is in the epigastrium; but pus may burrow and find its way down the flank, or among the muscles of the abdominal wall, and open perhaps at a point remote from the abscess cavity in the liver.

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Friction, both pleuritic and peritoneal, is sometimes to be made out, and is not without its value as a localising symptom.

Pneumonia, generally limited to the base of the right lung, and of a sub-acute and persistent character, indicates contiguity of the abscess to the diaphragm. It is especially common in those cases in which the abscess subsequently ruptures through the lung. This form of chronic pneumonia is a fruitful source of error in diagnosis.

Chronological relation of the hepatitis to the dysenteric attack.—This is most irregular and uncertain. In many cases of dysentery a concurrent hepatitis is manifest almost from the commencement of the attack; this hepatitis may not subside, but pass directly to abscess formation. Or the initial hepatitis and dysentery may both subside apparently, but the former may recur weeks, months, or even years afterwards, when, perhaps, the attack of dysentery is almost forgotten. Or there may be no active hepatic symptoms with the dysentery, hepatitis supervening only when all bowel trouble has long passed away. In a few cases no dysenteric history can be elicited; it is seldom, however, as has already been insisted on, that careful inquiry fails to bring out some story of previous bowel disturbance more or less urgent. In a few instances liver abscess of tropical origin does not declare itself until the patient has been several years resident in a temperate climate and quite outside the endemic area.

The *incidence of the symptoms* is equally variable. Some cases commence with marked sthenic fever, much local pain, great tenderness and hepatic enlargement, signs of suppuration, as rigor, hectic, and local bulging, rapidly supervening. Others, again, commence so insidiously that the patient can hardly say when he first began to feel ill; perhaps there may be a history of slow deterioration of the general health during a year or longer before definite hepatic symptoms show themselves. The former type seems to be the more common in the young and robust new-comer to the tropics; the latter, in the more or

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less cachectic and old resident. Between these extremes there is endless variety.

Duration of the disease.—Liver abscess may run its course in three weeks. Generally it is an affair of several months. Sometimes it may run on for a year or even longer; particularly so if it burst through the lung and drainage be imperfect, in which event the cavity may keep on bursting and refilling at intervals for almost an indefinite period. Occasionally a liver abscess becomes encysted and gives rise to no further symptoms, its existence being discovered only on the *post-mortem* table, the patient having died of quite another and independent disease.

Terminations. — Apart from operative interference, liver abscess may terminate in various ways. It may end in spontaneous rupture leading to death or recovery. Death may also be brought about in other ways—by the severity of the local disease; by prolonged hectic and exhaustion; by concurrent dysentery; or by intercurrent disease, as pneumonia, pulmonary abscess, empyema, peritonitis. Recovery may also ensue on the abscess becoming encysted or, possibly, absorbed.

Rupture of the abscess. — Rendu, in a series of 563 instances of abscess of the liver, compiled from various sources, gives an interesting table showing the direction of rupture in 159 of the cases which opened spontaneously. This table may be summarised as follows :—

Rupture occurred into the	pericardium in	1	case	0·13 per cent.
,,	pleura	31	,,	5·5 ,,
,,	lung	59	,,	10·5 ,,
,,	peritoneum	39	,,	6·9 ,,
,,	colon	6	,,	1 ,,
,,	stomach and duodenum	8	,,	1·4 ,,
,,	bile ducts	4	,,	0·7 ,,
,,	vena cava	3	,,	0·5 ,,
,,	kidney	2	,,	0·3 ,,
,,	lumbo-iliac region	6	,,	1 ,,

From this it will be seen that about 28 per cent. of

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liver abscesses rupture spontaneously, most generally into the lung or pleura.

Rupture into the lung.—If rupture takes place into the lung the abscess contents may be suddenly discharged, mouthful after mouthful of pus mixed with blood welling up or being coughed up. In a few instances, in such circumstances, death has occurred suddenly from the flooding of the lungs with pus. More commonly the discharge is effected gradually, a few drachms being brought up with each cough; in the aggregate this discharge may amount perhaps to five or ten ounces in the twenty-four hours. In favourable cases the daily amount expectorated gradually diminishes until all discharge ceases and the patient recovers. Frequently, however, a deceptive arrest of discharge and cessation of cough are followed by a rise of temperature, which had become normal on the occurrence of rupture. With this there may be a reappearance of the night sweats. In a few days cough and expectoration return as before and fever once more subsides. This process of alternate emptying and refilling of the abscess cavity may recur many times before recovery finally takes place. In some cases it continues for months, and may finally wear out the patient. Abscess may form in the lung; or a sudden and fatal hæmoptysis be brought about by ulceration opening some large pulmonary vessel. In some, expectoration never altogether ceases; if accompanied by fever this persistency indicates imperfect drainage, or, possibly, the presence of a second and unruptured abscess.

Characters of the expectorated liver pus.—The appearance of expectorated liver pus is almost pathognomonic. In colour it is chocolate brown; in consistence it is viscid and jelly-like. It may be streaked with blood; sometimes the expectoration may be almost entirely pure blood. Not unfrequently these hæmorrhagic cases are regarded and treated as examples of ordinary hæmoptysis. Presumably, in the majority of instances, this blood comes from the wall of an abscess jarred and torn by the succussion of the harassing cough. Under the microscope expectorated

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liver pus exhibits the appearance already described (p. 496).

Rupture into the pleura leads to sudden development of evidences of pleural effusion, which, unless relieved by drainage, may, in its turn, give rise to all the signs of empyema, and terminate in death, or in rupture through the lung or chest wall.

Rupture into the stomach is generally signalised by vomiting of the characteristic pus and, at all events temporarily, by cessation of local symptoms and fever.

Rupture into the bowel may cause diarrhœa, the pus, more or less altered, appearing in the stool. This is an occurrence that is frequently overlooked.

Rupture into the pericardium, or into a blood-vessel, is almost necessarily and rapidly fatal.

Rupture into the peritoneum is, of course, a serious occurrence, but, I believe, not necessarily fatal. The majority of liver abscesses, as will be presently described, do not contain the ordinary septic bacteria, and, therefore, may not give rise to septic peritonitis. I have seen recovery after this accident, the peritoneum having been well washed out and drained.

Rupture through the skin is said to be the most favourable, though a rare termination of liver abscess.

Mortality. — Rouis (203 cases), in Algiers, observed a mortality of 80 per cent.; Castro (125 cases), in Egypt, a mortality of 72·5 per cent., or, excluding cases operated on, of 76 per cent. In the Indian army, during the period 1891–94 (prior to which abscess of the liver, in the statistical returns, is not separated from hepatitis), and, presumably, including cases operated on, the mortality was 57·7 per cent.

Causes of death.—In Rouis's 162 fatal cases the causes of death are stated as follow: — Severity of the local disease, or through the associated dysentery, 125; bursting of the abscess into the peritoneal cavity, 12; into the pleura, 11; gangrene of abscess wall, 3; peritonitis, 3; pneumonia from effusion of liver pus into the lung, 3; rupture of adhesions, 2; pneumonia, 2; rupture into the pericardium, 1.

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Diagnosis.—Of all the grave tropical diseases none is so frequently overlooked as abscess of the liver. Acute sthenic cases are readily enough recognised; not so the insidious asthenic cases. The novice in tropical practice is some time in realising that grave disease of so important an organ as the liver may, for a long time, be unattended with urgent symptoms, whether local, or constitutional, or both.

The most common mistakes in diagnosis are: (1) Failure to recognise the presence of disease of any description, even when an enormous abscess may occupy the liver. (2) Misinterpretation of the significance and nature of a basic pneumonia—a condition so often accompanying suppurative hepatitis. (3) Attributing the fever symptomatic of liver abscess to malaria. (4) Mistaking other diseases for abscess of the liver and *vice versâ*—for example, hepatitis of a non-suppurative nature, such as that attending malarial attacks; suppurative hepatitis before the formation of abscess; syphilitic disease of the liver—softening gummata which are often attended with fever of a hectic type; pylephlebitis; suppurating hydatid; gall-stone and inflammation of the gall-bladder; subphrenic abscess; abscess of the abdominal or thoracic wall; pleurisy; encysted empyema; pyelitis of the right kidney; pernicious anæmia; leucocythæmia; scurvy and similar blood diseases associated with enlargement of the liver; ulcerative endocarditis; kala-azar; Malta fever; trypanosomiasis. Any of these may be attended with fever of a hectic type, increased area of hepatic percussion dulness, and pain in or about the liver.

Many times a correct diagnosis can be arrived at only by repeated and careful study of the case in all its aspects. Golden rules in tropical practice are to think of hepatic abscess in all cases of progressive deterioration of health; and to suspect liver abscess in all obscure abdominal cases associated with evening rise of temperature, and this particularly if there be enlargement of or pain in the liver, leucocytosis, and a history of dysentery—not necessarily recent dysentery. If doubt exist, there should be no hesitation

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in having early recourse to the aspirator to clear up diagnosis.

As bearing on prognosis, apart from the risk from sudden rupture in some untoward direction, to overlook abscess of the liver is a much graver error than to mistake some other disease for liver abscess; for the chances of recovery from operation are proportionately prejudiced by every day's delay.

Low pneumonia of the right base in a tropical patient should always be regarded with suspicion; in most instances it means abscess of the subjacent liver.

Perhaps the most common error is to regard the hectic of liver abscess as attributable to malaria. The regularity with which the daily fever recurs, the daily chilliness or even rigor coming on about the same hour, the profuse sweating, and other circumstances so compatible with a diagnosis of malaria, all contribute to this mistake. So common is the error that Osler says he hardly ever meets with a case of liver abscess which has not been drenched with quinine. My experience is the same. I have seen medical men make this mistake not only in their patients but in their own persons. If carefully considered, there are several circumstances which should obviate so serious an error. (1) No uncomplicated ague resists quinine in full doses. (2) In malaria, if the liver be enlarged the spleen is still more so; the reverse is the case in liver abscess. (3) The malaria parasite cannot be found in the blood in non-malarial hepatitis. (4) In liver abscess the fever is almost invariably an evening one; in malaria it most frequently comes on earlier in the day. (5) Quotidian periodicity, contrary to what is the case with tertian or quartan periodicity, is by no means pathognomonic of, or peculiar to, malaria. (6) The almost invariable history of antecedent dysentery, or, at least, of bowel complaint, in liver abscess. (7) Polymorphonuclear leucocytosis in liver abscess: mononuclear leucocytosis in malaria, kala-azar, and trypanosomiasis.

To mistake other forms of suppuration for liver

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abscess is of no great moment, because in many of the suppurative diseases just enumerated the treatment is the same as for liver abscess, and no bad result need be looked for if diagnosis is not quite accurate. A more serious error, however, is to overlook the presence of leucocythæmia, pernicious anæmia, or scurvy, and to proceed to aspirate an enlarged liver on the supposition that the symptoms arise from abscess. Fatal intraperitoneal hæmorrhage from the puncture has been known to ensue in such circumstances. If any doubt is possible on this point, a microscopic examination of the blood should be made before proceeding to explore.

A point to note in exploring is that, when the instrument enters the liver, an up-and-down pendulum-like movement will be communicated to the outer extremity of the needle, in harmony with the rising and falling of the organ in respiration. If the needle does not exhibit this movement, its point may be in an abscess cavity, but this abscess is not in the liver.

Treatment.—Hepatitis which has not proceeded to abscess formation should be treated, especially if dysentery be present or have been antecedent, with full doses of ipecacuanha, repeated once or twice a day for two or three days or longer, or by a cautious use of the purgative sulphates, and by poultices, rest, and low diet. Rogers has recently reiterated the value of ipecacuanha in such circumstances. If there be much pain, relief may be afforded by either wet or dry cupping over the liver, or by leeches around the anus. Ammonium chloride, in twenty-grain doses three times a day, is usually prescribed.

When the occurrence of rigor, or the development of hectic, or the appearance of local bulging, or the persistency of the fever and of the local symptoms, gives ground for suspecting that abscess has formed, active medication must be suspended, a somewhat improved dietary prescribed, and measures taken without unnecessary delay to locate by means of the aspirator the position of the pus.

When he proceeds to use the aspirator, the surgeon must be prepared to open and drain the abscess if pus

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be discovered; once diagnosis is established, nothing is gained by delay. By proceeding to open the abscess at once the shock of a double operation is avoided, and only one administration of the anæsthetic is required.

To facilitate aspiration, as well as the subsequent operation if such should be found to be necessary, the patient ought invariably to be placed under an anæsthetic. Unless in very special and exceptional circumstances, it is a mistake to attempt exploration without this, for the surgeon ought to proceed with deliberation and to feel himself at liberty to make as many punctures as he may think necessary. A medium- or full-sized aspirator needle should be used, as owing to the nature of the pus it may not flow through a cannula of small bore.

If there are localising signs, such as a tender spot, a fixed pain, a localised œdema, localised pneumonic crepitus, pleuritic or peritoneal friction, these should be taken as indicating, with some probability, the seat of the abscess and the most promising spot for exploratory puncture. If none of these localising signs is present, then, considering the fact that the majority of liver abscesses are situated in the upper and back part of the right lobe, the needle should, in the first instance, be inserted in the anterior axillary line in the eighth or ninth interspace, about an inch or an inch and a half from the costal margin and well below the limit of the pleura. The instrument should be carried in a direction inwards and slightly upwards and backwards and, if found necessary, to its full extent—3 to 4 inches. If pus be not struck the needle must be slowly withdrawn, a good vacuum being maintained the while in case the abscess has been transfixed and the point of the needle lodged in the sound tissue beyond. No pus appearing in the aspirator, the remainder of the dull hepatic area must be systematically explored, both in front and behind, regard being had to the lung and pleura on the one hand, and to the gall-bladder, large vessels, and intestine on the other. The peculiar colour—often like dirty brown thick blood—of liver pus must not be allowed

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to deceive the operator into thinking that he has failed to strike the abscess.*

At least six punctures should be made before the attempt to find pus is abandoned. Provided there is complete absence of breath sounds, of vocal fremitus and resonance over the lower part of the right lung, and pus has not been reached from lower down, then the pleura or lung may be disregarded and puncture made anywhere below the line of the nipple and angle of the scapula, or wherever the physical signs suggest.

The surgeon should be encouraged to make early use of the aspirator by the fact that its employment, even where no pus is discovered, is not unfrequently followed by rapid improvement in all the symptoms. Many such cases are on record. Hepatic phlebotomy, as Harley designated the removal from the liver of a few ounces of blood by the aspirator needle, is a measure of proved value in hepatitis. With due care, risk from hæmorrhage is small; it is very small indeed in comparison with the risk of allowing an hepatic abscess to remain undiscovered and unopened.

Some surgeons, in order to obviate the small risk from hæmorrhage attending aspiration through the abdominal or chest wall, prefer to expose the surface of the liver by a short incision and then explore.

It is hardly necessary to add that strict aseptic precautions, in the way of purifying the patient's skin, the surgeon's hands, and all instruments, must be carefully observed.

Operation for abscess of the liver.—The following is the operation usually practised by English surgeons. It is substantially that described by Godlee in the *British Medical Journal* of January 11th, 1890, to which the reader is referred for many valuable details and practical hints.

If pus is struck below the costal border, the aspirator needle being left *in situ* as a guide, the

* I have seen the peculiar brownish fluid resulting from the action on blood of the carbolic lotion that had been used to sterilise the exploring syringe, mistaken for pus. To obviate so grave a mistake, the exploring syringe should be washed out with boiled water before use.

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abdominal wall is incised down to the peritoneum. A three-inch incision will give plenty of room. If firm adhesions be discovered, a sinus forceps is at once run along the needle, and pushed through the intervening liver tissue and into the abscess. The aspirator cannula is now removed, and the blades of the forceps are opened sufficiently, as it is being withdrawn, to make a wound in the liver big enough to admit the fore-finger, which must now be inserted and moved about so as to enlarge the wound and to gain some idea as to the size and direction of the cavity of the abscess. A rubber drainage-tube, about as large as the finger, and provided with a flange, is cut to a suitable length, and carried by means of the forceps to the back of the abscess. The abscess is then allowed to empty itself. When pus no longer flows freely, a massive antiseptic dressing is applied and firmly secured by a broad binder or many-tailed bandage.

If, after division of the abdominal wall, no reliable adhesions be discovered between this and the liver, the capsule of the latter must be securely attached to the former by a double circle of stitches. The abscess is then to be opened, as above described, with sinus forceps. After stitching, some surgeons prefer, before opening the abscess, first to stuff the wound in the abdominal wall with iodoform gauze, and to wait for a day or two for adhesions to form. Others stuff the wound with gauze without previous stitching.

Should the abscess be struck through an intercostal space, and if the latter be not deemed sufficiently wide to admit of manipulation and free drainage, a couple of inches of rib had better be excised. The diaphragm may then be stitched to the thoracic wall or, better, to the skin as well, when the abscess may be opened with forceps. To stitch the capsule of the liver to the diaphragm is a somewhat difficult proceeding; but if there are no reliable adhesions it had better be attempted, especially if the opening is to be made through a part of the liver covered by the peritoneum. If by any chance the pleura is opened during the operation, pneumothorax will result, an unfortunate, but not necessarily a

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serious, contingency. In this case the hole in the pleura must be carefully stitched in such a way that the pleural cavity is completely cut off before the diaphragm is divided and the abscess opened. Pus must not on any account be allowed to enter the pleural cavity; this, owing to the aspirating influence of inspiration, it would readily do if the smallest hole should remain patent. The young surgeon would do well to practise these operations on the dead body, and familiarise himself with the relations of the various structures involved.

Some operators of experience completely ignore the absence of peritoneal adhesions, and, even in these circumstances, open the abscess without previous stitching of peritoneal surfaces. The risk and danger of escape of pus into the peritoneal cavity, they hold, is very small if free drainage to the outside is secured. Macleod considers that, in the circumstances, stitches will not hold in the soft and inflamed liver tissue; he also considers that, in the event of the incision having to be made in the thoracic wall, removal of part of a rib is unnecessary. On account of the liability of a rubber drainage-tube to become nipped when the emptying sac causes a want of correspondence between the wound in the abdominal or thoracic wall and that in the liver, and, also, on account of facility of introduction during the subsequent dressings, this operator uses metal drainage-tubes of suitable lengths—four inches, three and a quarter inches, two and a half inches, and one and three-quarter inches—with an oval lumen of four-tenths by three-tenths of an inch. These tubes he introduces by means of a special guide.

The author's method.—The following easy, rapid, and efficient method of operating on abscess of the liver I have frequently practised, and can recommend. The necessary apparatus (Fig. 63), which can be made by native workmen, consists of a large trocar and cannula (*a*), four to five inches long, by three-eighths of an inch in diameter; a steel stilette (*b*) at least fourteen inches in length; two metal buttons (*c*, *d*) a quarter of an inch at their greatest diameter, with

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long (half-inch), hollow, roughened necks into which the ends of the stilette fit loosely; six inches of half-inch stout drainage tubing (*e*). While the ends of the drainage tubing are held and well stretched by an assistant, they are firmly lashed to the stem of the buttons, over the ends of the shorter (*d*) of which, for additional security, the tubing is also tied (*e*). Two large holes, to provide for free drainage, are then cut

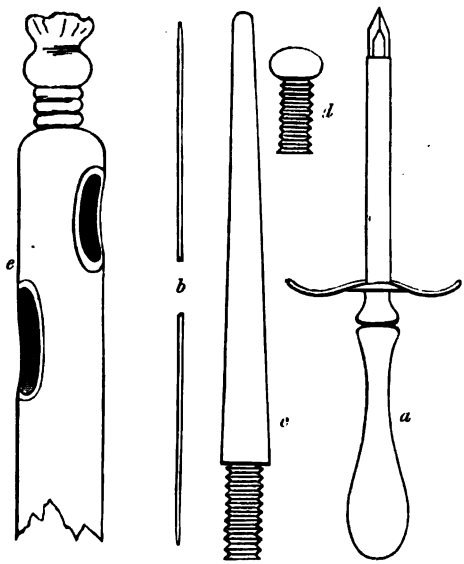

Fig. 63.—Apparatus for operation for abscess of the liver (*a* and *b* reduced).

close to one end of the drainage-tube. The tube is then mounted on the stilette by inserting one end of the latter through one of the drainage holes and lodging it in the hollow neck of the distal button (*c*), and thereafter so stretching the rubber that the other end of the stilette can be inserted into the neck of the other button (*d*). When thus stretched, the drainage-tube should be capable of passing easily through the cannula. The apparatus being so prepared and

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rendered thoroughly aseptic by soaking in carbolic lotion, and the direction of the abscess and its depth from the surface having been carefully ascertained by means of the aspirator and noted, the aspirator is withdrawn and an incision, about an inch in length, made through the skin at the site of the puncture. The trocar and cannula are then thrust into the abscess and the trocar withdrawn. After allowing a small quantity of pus to escape, so as to relieve any tension that may be present in the abscess sac, the stretched drainage-tube, perforated end first, is slipped into the cannula and carried to the back of the abscess. Holding the stretched drainage-tube firmly, and maintaining it carefully in contact with the back of the abscess with one hand, withdraw the cannula with the other. Still grasping the drainage-tube firmly, the button on the free end of the apparatus is slipped off the stilette, the end of which is made to perforate the drainage-tube close to the button. This it readily does, and the drainage-tube is allowed slowly to resile towards the fixed end still held in contact with the back of the abscess. When the drainage-tube has completely contracted, the stilette is withdrawn. The drainage-tube is then transfixed with a safety-pin inserted close to the skin, and the superfluous tubing cut off. Pus flows freely from the tube, which now firmly plugs the wound in the abdominal wall and liver, and bridges the peritoneal cavity. When the abscess has nearly emptied itself the usual antiseptic dressing is applied. In operating through the thoracic wall, if deemed desirable, part of a rib may be excised before the trocar is introduced.

I claim for this operation that it is easily done, and that it may be undertaken by the merest tyro in surgery and in the absence of skilled assistance; that there is no risk from bleeding; that, the peritoneum being bridged across by the drainage-tube which is securely grasped by the liver tissue, there is no risk of escape of pus into the peritoneal cavity; that in a very short time lymph is effused around the tube,

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giving additional security when, after a time, the tube has become loose; that, if deemed necessary, a larger drainage-tube, by stretching it on the stilette in the same way as described, can be substituted for the half-inch tube; that an abscess deep in the liver can be as readily opened, and with as little risk, as one lying near the surface; that the shock is much less than in the cutting and tearing operation; that there is no risk of pneumothorax should the pleural cavity be traversed; and that the drainage obtained is equal to that secured by any other method of operating. Several of my surgical friends have adopted this method of operating, and have expressed great satisfaction with the ease with which it is performed, and with the results.

Other operations. — Some Continental surgeons recommend extensive incision of the liver, using a Paquelin's knife with the view of minimising bleeding. Zancarol, for example, advises that the hepatic and integumental incisions should extend the whole breadth of the abscess cavity, which he mops out and stuffs with iodoform gauze. Certain French surgeons recommend scraping the abscess cavity; most practise irrigation with some antiseptic fluid. These methods do not find favour with English or Indian surgeons.

The method of opening the abscess by caustics, formerly much in vogue, is now abandoned; equally so another method, also formerly employed—namely, that of leaving a rigid trocar in the wound.

Treatment after operation.—For the first few days after a liver abscess has been opened the discharge is considerable, and the dressing may have to be changed frequently. Very soon, however, should the case do well, the discharge rapidly diminishes, and the dressing requires renewal only every other day or every three or four days. During the first week the drainage-tube, provided it be acting efficiently, should not be disturbed, more particularly as it may be difficult to replace. Later, it may be removed and cleaned, and when discharge has practically ceased, cautiously shortened. *It is a great mistake to begin shortening*

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the tube before it is being pushed out, or so long as there is any appreciable discharge. If there is the slightest indication, such as rise of temperature, that pus is being retained, the drainage must be rectified and the sinus, if necessary, dilated with forceps and finger, and a full-sized drainage-tube introduced as far as it will go. If this does not suffice, a counter-opening may have to be made. *Delay in remedying imperfect drainage is a serious, it may be fatal error.*

Should an abscess on being opened be found to be septic, or should it become so, it must be flushed out daily, or twice a day, with a weak non-mercurial antiseptic, and a counter-opening made if necessary. Quinine solution—1 in 1,000—is useful if much amœba-laden discharge persists for a length of time.

After liver abscess has been opened and is draining well, temperature rapidly falls and, in a few days or almost at once, becomes normal. Should fever persist, it is to be inferred either that the drainage is inefficient, or that there are more abscesses in the liver, or that there is some complication. If it be deemed that there is another abscess, this should be sought for with the aspirator, and, if found, opened and drained. I have seen a patient recover after three abscesses had been so treated.

Treatment of abscess discharging through the lung.—In the case of abscess discharging through the lung, and not progressing favourably, the question of obtaining by surgical means more efficient drainage must be considered. There are two possibilities which render interference desirable. (*a*) Continued discharge of pus and blood, with or without attendant hectic; a condition which, if it persist, will, in all probability, in the end kill the patient. (*b*) Not unfrequently prolonged discharge through the lung may induce fibrotic changes in that organ, or may give rise to pneumonia, or to abscess of the lung with all its attendant dangers, such as thrombosis or abscess of the brain.

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In these circumstances it is sometimes difficult to arrive at a decision as to whether an attempt should be made to open and drain the abscess, or to leave it alone. A large proportion of the cases recover, but at least an equally large number die. Of the latter, a proportion may certainly be saved by timely surgical interference.

In all cases of abscess discharging through the lung a careful register should be kept of three things —body temperature, daily amount and character of expectoration, and, once a week, the weight of the patient. If temperature keeps up, if the amount of pus continues the same or increases, or if the patient continues to lose weight, an attempt should be made at all risks to reach and drain the abscess from the outside. If temperature keeps normal, if pus gradually or intermittently decreases, and if the body-weight is maintained or increases, operation is unnecessary, or, at all events, should be deferred.

In exploring the liver in such cases it must be borne in mind that most likely the abscess cavity is collapsed, and that the sides of the abscess may be in contact. Such an abscess is not likely to be discovered unless the needle be thrust in to its full extent, and, whilst a good vacuum is being maintained in the aspirator, slowly withdrawn. If by good fortune the abscess has been traversed, then, when the end of the needle crosses the cavity, a small amount of pus will be seen to flow. Great care must now be exercised to keep the needle in position so as to serve as a guide in opening the abscess. Recovery has been known to follow the introduction of a drainage-tube in the presumed direction of such an abscess, even although the abscess cavity was not entered, much less drained by the tube.

Treatment of abscess rupturing into a serous cavity.—When there is evidence that an abscess of the liver has ruptured into the peritoneum, into the pleura, or into the pericardium, the particular serous cavity involved must be opened at once and treated on general surgical principles; otherwise, the patient will almost surely die. In the circumstances

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the surgeon will be justified in assuming great risks.

The *prognosis in early operations* on single abscess of the liver, provided there is no dysentery or other complication, is good. In multiple abscess, or in single abscess if there is active dysentery or other serious complication, prognosis is bad. In multiple abscess, if there are more than two or three abscesses, it is necessarily hopeless.

The *question of return to the tropics* after recovery from liver abscess frequently crops up. If feasible, and if the patient has not to make too great a sacrifice, he ought to remain in a temperate and healthy climate. There are many instances, however, of individuals who have enjoyed permanent good health in the tropics after recovery from liver abscess.

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CHAPTER XXXIII

INFANTILE BILIARY CIRRHOSIS

WITHIN the last two decades, a peculiar disease of the liver has been noticed in children in Calcutta and, to a less extent, in other large towns of India. It is found to be more prevalent in Hindoo than in Mahomedan children. Thus, in Calcutta, from 1891 to 1893 inclusive, infantile biliary cirrhosis, the name given to this disease, caused 1,748 deaths. Although the Hindoo and Mahomedan populations of that city are about equal, yet as many as 1,616 of the deaths occurred in Hindoos, whilst only eighty occurred among Mahomedans, the balance of the mortality being among the Eurasians and other races. The disease occurs principally in children under one year, rarely attacking those over three years. As a rule, it commences during dentition, or about the seventh or eighth month, running a fatal course in from three to eight months. In rare cases it may commence within a few days of birth. Instead of lasting several months, its progress may be much more rapid, and terminate in death in from two to three weeks.

The cause of infantile biliary cirrhosis is quite unknown. Neither alcohol, syphilis, nor malaria has anything to do with it. The children of the well-to-do are relatively more frequently attacked than those of the poor. It has also been observed that it tends to run in families, child after child of the same parents succumbing within a year or two of birth. In 400 cases Ghose had only six recoveries; in some of these recoveries the diagnosis was doubtful.

Symptoms.—Commencing insidiously, the characteristic initial enlargement of the liver may have made considerable progress before the disease is suspected. Nausea, occasional vomiting, sallowness,

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feverishness, constipation, anorexia, irritability of temper, thirst and languor call attention to the child's condition. On examination, the liver is found to be enormously enlarged, extending perhaps to the umbilicus or even lower. The surface of the organ is smooth; the edge, at first rounded and prominent, as the liver begins to contract becomes sharp and distinct and can be readily grasped between the fingers, the swollen organ feeling hard and resistant. Fever of a low type sets in; the sallowness deepens into profound jaundice; the stools are pale, the urine is dark; and there may be ascites, with puffiness of the feet and hands. Sooner or later, death from cholæmia ensues.

Pathological anatomy and pathology.—Surgeon-Major Gibbons, who has given an elaborate and most careful account of the pathological anatomy of this disease, concludes that it is a peculiar form of biliary cirrhosis, the consequence of the action on the liver cells of some irritant of gastric origin, which leads to degeneration of the cells in the first instance, with subsequent increase of intercellular connective tissue and, later, of the portal sheaths. The formation of new bile ducts between the hepatic cells, which is a well-marked feature, he regards as evidence of a natural curative effort having for its object a regeneration of the liver cells.

Treatment.—Hitherto, in this disease, treatment has been of little avail. There is some ground, however, for thinking that early removal from the endemic locality, and a complete change of wet-nurse and food, might have a beneficial effect.

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CHAPTER XXXIV

PONOS

Under the name "Ponos" Karamitsas and Stephanos have described a peculiar disease endemic in the exceedingly insanitary and poverty-stricken islands of Spezzia and Hydra in the Grecian Archipelago. Ponos, in a sense, is analogous to the infantile biliary cirrhosis of Indian cities. Like the latter, it is confined to very young children, it is endemic in particular districts, tends to run in particular families, to pursue a more or less chronic course, and is invariably associated with disease of an abdominal viscus—in this case the spleen. Though not invariably so, it is usually fatal.

Symptoms.—Commencing somewhat suddenly and, commonly, during the first year of life, the earliest symptoms to attract the attention of the parents are languor and a pallor which rapidly acquires a sallow tint. Fever of an irregular character sets in; the spleen enlarges; prostration is very marked; and, it is said, the urine exhales a peculiarly disagreeable odour. Emaciation becomes progressive. Although the digestion is enfeebled and constipation is nearly always present at first, the appetite is fairly preserved, though it may be perverted or excessive. The spleen gradually attains a great size, and is tender—hence the name, "ponos" (pain). The associated fever is of an irregular character, tending to become remittent, the thermometer rising during the exacerbations to 39° or 40° C.; towards the end the fever assumes hectic characters. Complications in the form of bronchitis, pneumonia, diarrhœa, dysentery, peritonitis, or meningitis may show themselves. When the disease has been established for some time œdema and ascites may occur, and there may be hæmorrhages in or from various organs, especially the gums. In

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certain cases boils, and even patches of superficial gangrene, are met with. The progress of the disease is very variable; it may last from one or two months to one or two years.

Pathological anatomy and pathology.—Of these nothing is known further than that, besides enlargement of the spleen, ponos exhibits none of the characteristic lesions of tuberculosis, syphilis, rickets, leukæmia, splenic anæmia or of malaria. Its cause is quite unknown. Its remarkably limited endemicity and (if the observation be correct) the presence of a pronounced leucopenia suggest a protozoal germ similar to that of kala-azar. It has been remarked, that it is prone to occur in the children of those who have themselves suffered in infancy in the same way, suggesting house infection. It is said that in the case of the disease attacking the child of a tuberculous mother, recovery will very promptly set in if the child be supplied with a healthy wet-nurse. It has been suggested that ponos is an expression of malaria, but the *post-mortem* evidences are altogether against this supposition; moreover, malaria is said to be unknown in the two islands in which this peculiar disease is endemic. Ponos affects the children of rich and poor alike, and those living in good as well as those living in dirty, unhygienic houses. It has not appeared on the mainland of Greece and is decreasing in the endemic area, where it seems to have appeared suddenly about 1835.

Treatment.—No specific is known. Quinine, tonics, fruit juices, careful management of the food, and early change of residence would seem to be indicated.

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SECTION IV.—INFECTIVE GRANULOMATOUS DISEASES

CHAPTER XXXV

LEPROSY (*Elephantiasis Græcorum*)

Definition.—A chronic infective granulomatous disease produced by a specific bacterium, and characterised by lesions of the skin, nerves, and viscera eventuating in local anæsthesia, ulceration, and a great variety of trophic lesions. After a long course it is almost invariably fatal.

History.—The many allusions in the oldest Chinese, Indian, Syrian, and Egyptian writings to a chronic, disfiguring, and fatal affection possessing well-marked and characteristic skin lesions, warrant us in concluding that the disease now known as leprosy was as common and familiar in the East in times of remotest antiquity as it is at the present day.

There is some evidence—necessarily of a negative character—that leprosy is of comparatively recent introduction into Europe. The earlier Greek and Latin writers do not mention the disease. Hippocrates, who, had he been practically acquainted with leprosy, would undoubtedly have described it accurately and fully, makes but brief allusion to the subject. Aristotle is the first of the Greek writers to give an unequivocal description. We may infer, therefore, that the introduction of leprosy into Greece probably took place between the time of Hippocrates and that of Aristotle—that is to say, between 400 B.C. and 345 B.C. Most likely it came from Egypt. In the time of Celsus—53 B.C. to A.D. 7—it was still a rare disease in Italy; but, during the earlier centuries of our era it increased there, and, probably following in the wake of the Roman conquests, it appears to

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have spread thence over the greater part, if not over the whole, of Europe. By the end of the seventh century it was well known in Spain, France, and Lombardy. There is a notice of its occurrence in Ireland in 432. As regards England, the first allusion to leprosy refers to about the year 950. The popular idea that it was brought to this country from the East by the returning Crusaders (*circa* 1098) is therefore incorrect; though, doubtless, the Crusaders, and the multiplicity of pilgrimages so much the fashion in the Middle Ages, and the destitution arising from the many wars of the period, had something to do with its rapid diffusion and great increase about this time.

So common was leprosy during the Middle Ages that the rulers and clergy of nearly all European states, becoming alarmed at its rapid extension and terrible ravages, took measures, by instituting leper asylums and enacting stringent laws for the segregation and isolation of lepers, to restrict the spread of what was speedily becoming almost a general calamity. These measures, based on what we now know to be a correct appreciation of the infectious nature of the disease, were ultimately crowned, in the case of most European countries, with almost complete success. Reaching its acme during the fourteenth century, leprosy then began to decline, although as regards Great Britain it did not finally disappear as an indigenous disease until the end of the eighteenth century. It died out first in England, later in Scotland—the last British leper dying in Shetland in 1798. In Italy, France, Spain, Germany, and Russia the repressive measures were almost equally successful, although in these countries, in Greece, and in the Greek islands leprosy of indigenous origin is still occasionally to be seen. The only country in Northern Europe in which at the present day it may be said to linger to any extent is Norway, where, in places, it is still by no means uncommon (in 1890 there were 1,100, in 1906 under 500 known lepers); but even here, under a system of segregation and comparative isolation—more humane perhaps in its application than that

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practised by our ancestors, although identical with it in principle—the disease is rapidly dying out.

Apart from Egypt, we know nothing of the early history of leprosy in Africa. We are equally ignorant as regards aboriginal America. The historians of the Spanish Conquest do not allude to it as a native disease; we appear, therefore, to be justified in concluding that the introduction of leprosy into the New World was probably effected by the Spaniards, or through the negroes in the days of the slave trade.

Rise of modern knowledge of leprosy.—The more important landmarks in our modern knowledge of leprosy are, first, the publication in 1848 of Danielssen and Boeck's *Traité de la Spedalskhed*, in which, for the first time, the clinical features of the disease were carefully and critically described; second, the descriptions of the macroscopic and microscopic lesions—the leproma, the nerve lesions, and the lepra cell—by Virchow, Vandyke Carter, and many others; and last, the discovery in 1874 by Armauer Hansen of the specific cause of leprosy—the *Bacillus leprœ*—a discovery which brings this disease into line with tuberculosis, and has given a much-needed precision to our ideas on the important subjects of heredity and contagion, and on other practical points bearing on the question of the leper as a source of public danger and on his treatment and management.

Geographical distribution.—Whatever may have been the case formerly, at the present day, with unimportant exceptions, leprosy is a disease more particularly of tropical and sub-tropical countries. So generally is it diffused in these that it would be more easy to specify the tropical countries in which leprosy has not, than to enumerate those in which it has been ascertained to exist. Moreover, it is probable that in many of the countries not yet positively known to harbour the disease it does really exist; for experience shows that the endemic area of leprosy enlarges as our knowledge of the natives of the uncivilised regions of the earth becomes more intimate. It may be safely concluded, therefore, that with the exception of a few insig-

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nificant islands, leprosy is an element, and often an important element, in the pathology of nearly all warm countries.

The only tropical country of any magnitude about which we have anything like accurate leprosy statistics is India; and even in this instance the figures, for many reasons—principally errors in diagnosis and concealment—are untrustworthy. According to the census of 1891, after making allowance for error, it is estimated that in British India there were 105,000 lepers in a population of 210,000,000—a ratio of about 5 in 10,000. Respecting China, of all countries probably the one in which there is the largest number of lepers, we have no figures to go by; but, judging from what is seen in the coast towns and treaty ports, the number of lepers is probably sensibly greater than in India. In Japan, in the Philippines, in Cochin China, in the Malay peninsula, in the islands of the Eastern Archipelago and of the South Pacific, in Persia, Arabia, and Africa, the disease is common enough. The same may be said of the West Indies and of the tropical regions of America.

As regards more temperate countries, we know that there are a considerable number of lepers at the Cape, a few in Australia (principally Chinese but also a few Europeans), a few in San Francisco (Chinese). In Canada and in the United States there are also a few lepers of European blood, but their number is quite insignificant. In New Zealand, where leprosy was at one time common among the Maoris, it has died out. There are a good many lepers in Iceland. It is also reported as existing among the aborigines of the Aleutian peninsula and Kamschatka. In Great Britain and other European countries, particularly in the capital cities, lepers are not unfrequently exhibited at medical societies; but, with rare exceptions, these cases are not of indigenous origin, most of them having contracted the disease abroad.

Though thus extensively diffused, leprosy is by no means equally prevalent throughout the wide area indicated. Thus in China it is comparatively rare in

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the northern provinces, excessively common in the southern. In India a similar caprice of distribution is noted; in Burdwan, for example, the proportion of lepers in 10,000 of the population is as high as 19·5, whereas in several other districts it is as low as 1·5, or even lower. This caprice of distribution does not seem to depend directly on climate, geological formation, or suchlike physical conditions; for leprosy is found in mountainous districts, on the plains, on the coast, in the interior, in all varieties of climate, and on all kinds of geological strata. Social conditions, it would seem, have most to do in determining distribution; its endemic prevalence appearing to be bound up in some way with uncleanly habits, squalor, dirt, and poverty —not, be it noted, directly caused by these things, but associated with them.

Recent introduction.—An interesting and, from the ætiological standpoint, an important circumstance about the geographical distribution of leprosy is its appearance and rapid spread in recent times in certain islands whose inhabitants, there is good reason to believe, had previously been exempt. This modern introduction of leprosy into virgin soil, so to speak, has taken place in the Sandwich Islands, in New Caledonia, and elsewhere.

Sandwich Islands.—In the case of the Sandwich Islands leprosy was noted among the aborigines for the first time in 1859. After the most painstaking investigation Dr. Hildebrand failed to trace it farther back than 1848. Soon after its presence was recognised the disease spread so rapidly that by the year 1865 there were 230 known lepers in a population of 67,000. By 1891 the native population, from various causes, had diminished to 44,232; of these 1,500 were lepers—about 1 in 30.

New Caledonia.—In New Caledonia leprosy was unknown until 1865. It is supposed to have been introduced about that time by a Chinaman; the man was well known. Its rapid diffusion throughout the island can be, and has been, traced step by step. In 1888 the lepers numbered 4,000.

Isle of Pines.—Similarly, in the Isle of Pines

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leprosy was introduced in 1878, and has since spread. In the Loyalty Islands the first case was seen in 1882; in 1888, in the island of Mare alone, there were 70 lepers.

Symptoms.—Although, as will afterwards be explained, the *Bacillus leprœ* is the cause of all leprosy, the clinical manifestations of its presence are far from being identical in every case; indeed, they are almost as varied as are those of syphilis or of tubercle. Our early conceptions of the disease, derived for the most part from the Bible or poetical literature, in which the leper is symbolical of all that is loathsome and hopeless, are apt to mislead. As a matter of fact, in its earlier stages leprosy is far from being always, or even generally, a striking disease. Often for years the only visible evidence of its existence may be two or three small blotches, or perhaps one or two patches of pale or pigmented skin on trunk or limbs—very likely concealed by the clothes and perhaps disregarded by the patient himself—the true significance and nature of which can be appreciated only by the expert. It is generally not until the later stages that we see the disfiguring and extensive lesions on which the popular conception is founded. As a rule, leprosy is a disease of very slow development. Sometimes, it is true, it is suddenly and frankly declared from the outset, and progresses rapidly; but in the vast majority of cases the early lesions are trifling and are apt to be misinterpreted and overlooked, and years elapse before serious mutilation or deformity is produced. The student must bear this important practical fact in mind in the study and diagnosis of all equivocal skin lesions in persons residing in or coming from the endemic haunts of leprosy.

To facilitate description, it seems advisable to divide the evolution of leprosy into stages, premising, however, that the division proposed is in great measure an artificial one. What are here designated stages are not, all of them, clinically and in every instance, abruptly separated or even present; for the most part they merge imperceptibly into each other

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and, in not a few instances, some of them cannot be recognised.

1. Primary infection.
2. Period of incubation.
3. Prodromata.
4. Primary exanthem or macular stage.
5. Period of specific deposit.
6. Sequelæ — ulceration, paresis, trophic lesions.
7. Terminations.

1. *The primary infection.*—Seeing that leprosy is caused by a specific germ, there must have been a time, in the history of every leper, when the infecting germ entered the body. In many specific diseases, such as syphilis, the site of the primary infection is indicated by a well-marked local lesion, and the time of infection can usually be ascertained. So far as present knowledge goes, this much cannot be affirmed of leprosy; in this disease we know of nothing that indicates precisely either the seat or, with rare exceptions, the time of primary infection. In this respect leprosy resembles tuberculosis. We are equally ignorant as to the condition of the infecting germ, whether it enters the body as spore or as bacillus, and also as to the medium in or by which it is conveyed. We cannot say whether it enters in food, in water, in air; whether it passes in through the unbroken epithelium, or whether it is inoculated on some accidental breach of surface, or, perhaps, introduced by some insect bite.

Recently Sticker found *Bacillus leprœ* in the nasal mucus in 128 out of 153 lepers examined. He considers that the initial lesion of the disease is a specific ulceration of the cartilaginous septum of the nose; the lesion persists and is an active source for the diffusion of infection. Of the presence of this condition, epistaxis, he maintains, is often an early symptom. Several subsequent observers favour this view.

Although we are in absolute ignorance as to the process of infection, we may be quite sure that in leprosy there is an act of infection, and that the

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infective material comes from another leper. Leprosy has never been shown to arise in a country *de novo*. There are many facts and arguments to support this statement; their discussion is deferred until the subjects of heredity, contagion, and the hygienic questions connected therewith, come to be considered.

2. *The period of incubation.*—This is generally, possibly always, long, and has to be reckoned usually in years—two or three at least. There are cases on record in which the period of incubation must have been longer even than this. Danielssen mentions one in which the period was ten years, Leloir describes another in which fourteen years or more, and Höegh one in which twenty-seven years elapsed between the time at which infection was presumed to have occurred and the first manifestations of the disease. On the other hand, cases are on record in which the incubation period was set down at three months or even at a few weeks.

3. *Prodromata.*—Fever of greater or less intensity, and occurring more or less frequently is, almost invariably, a feature of the prodromal stage of leprosy. Febrile attacks may recur off and on during one or two years. It is well to bear in mind that in tropical countries such attacks are apt to be looked on as malarial. Another very common prodromal feature is an unaccountable feeling of weakness, accompanied usually by a sensation of heaviness and a tendency, it may be irresistible, to fall asleep at unusual times. Dyspeptic troubles, associated with diarrhœa in some cases, with constipation in others, and usually attributed to "liver," are also common. Epistaxis and dryness of the nostrils, perhaps symptomatic of the initial lesion, perhaps corresponding to the epistaxis in the prodromal stage of typhoid, tuberculosis, and such as is sometimes met with in early syphilis, are noted by Leloir. Headache; vertigo; perversions of sensation—such as localised pruritus, hyperæsthesia, "pins and needles," neuralgic pains—intermittent for the most part, and perhaps very severe and especially common in the limbs and face; general aching, rheumatic-like pains in loins,

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back, and elsewhere; all or any of these for months may herald the explosion of unequivocal leprosy.

Another curious feature in early leprosy, also noted by Leloir, is the liability in many instances to excessive sweating, which comes on without apparent, or on very slight provocation. I had once under observation an Englishman who subsequently developed leprosy, in whom this prodromal symptom was particularly pronounced, so pronounced that he had remarked it himself. This gentleman for many years kept a diary in which, among other things, he recorded very carefully matters relating to his health; so that it was easy to trace from this diary the gradual evolution of his leprosy. The first unequivocal manifestation of the disease, an extensive erythematous patch on the ulnar side of the left arm and hand, which afterwards became anæsthetic, and two or three pigmented spots on the cheek, back, and leg, was noted on March 3rd, 1894. Five years before this there is an entry in his diary, under date June 4th, 1889, of the first of a long series of severe headaches, transient febrile attacks, and progressive deterioration of health and vigour. Under date of June 9th, 1892, is the first mention of the profuse perspiration which, occurring without obvious cause, continued to be a prominent feature until several months after the appearance of the skin lesions referred to. In the diary such entries as the following frequently occur: "Nov. 20th, 1892.—Feel poorly and sweating inordinately; wondering what is coming over me. I am very ill." "Dec. 5th to 19th, 1892.—Ill in bed. I had furious sweats during this time, and had dreadful pains in the back, lower part." And again: "Dec. 21st, 22nd.—Feeling very ill: awful sweats; weak; done up." As pointed out by Leloir, this hyperidrosis may be general or it may be confined to particular parts, generally the trunk, the limbs being unaffected or even being the subject of anidrosis. A still more limited anidrosis is sometimes noted; it usually happens that these non-sweating spots become anæsthetic at a later period of the disease.

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Just as in syphilis, in a very small proportion of cases of leprosy there is a complete absence of constitutional symptoms prior to the appearance of the specific skin eruption.

4. *The primary exanthem.*—In a considerable proportion of cases, after a longer or shorter period of indifferent health, sometimes preluded by an outburst more severe than usual of fever and other prodromal phenomena, an eruption appears on the skin. This generally coincides with, or is soon followed by an improvement in the general health.

Although strictly macular, this eruption—the primary exanthem of leprosy—varies in different cases as well in respect of the size of the spots as of their number, duration, and other characteristics. They may be no larger than a millet seed, or they may occupy surfaces many inches in diameter; they may be numerous, or there may be only two or three. The earlier spots are usually purely erythematous, disappearing on pressure, and being darkest in the centre and shading off towards the periphery. But in some cases they may be pigmented from the outset; or they may be mere vitiliginous patches; or all three forms of macula may concur in the same individual—erythematous, pigmented, and vitiliginous. In not a few lepers what in the first instance was an erythematous patch may in time become pigmented, or it may become pale; in the latter case the loss of pigment is usually associated with a certain degree of atrophy of the cutis. Or it may be that the centre of an erythematous patch clears up, the periphery of the patch remaining red and perhaps becoming pigmented; so that the affected spot comes to present the appearance of a red or dark ring, or portion of a ring, enclosing a patch of pale, usually anæsthetic skin. In certain instances the eruption of the various forms of maculæ may be preceded by local paræsthesiæ, such as a sense of burning, tingling, pricking, and so forth.

At first the maculæ may be evanescent and may fade wholly or in part in the course of a few days, weeks, or months; but as the disease progresses, and

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fresh spots appear, they tend to greater permanency, to be more liable to pigmentation, and are partially or wholly anæsthetic from the outset, or subsequently become so.

A striking feature in this and in all leprous eruptions is the loss of the hair in the affected areas. Another striking circumstance is the fact that the most hairy part of the body, the scalp, is never or very rarely affected either with leprous eruptions or with leprous alopecia. As the face, particularly the superciliary region, is prone to all forms of leprous eruption, falling of the eyebrows is a very usual, very early, and very characteristic phenomenon. The beard, too, is apt to be patchy, particularly in nodular leprosy. In many instances, before they drop out, the individual hairs become white, or downy, or splintered, or monillated.

The most frequent seats of the primary macular eruption are the face, especially the superciliary region, the nose, cheeks, and ears; the extensor surfaces of the limbs; the backs of the hands; the back, buttocks, abdomen, and chest. The palms of the hands and the soles of the feet are rarely if ever attacked. At this stage of the disease the mucous membranes are very rarely affected.

In the distribution of the maculæ a rough symmetry may or may not be discernible.

5. *The period of specific deposit.*—During the stage just described, if there be any thickening of the skin or other evidence of new growth, it is barely perceptible to sight and but slightly so to touch. Sooner or later, however, another stage is entered on, a stage characterised by the deposit or, rather, growth of a tissue possessing well-marked specific characters. This deposit occurs either in the skin, or in the continuity of the peripheral nerve trunks, or in both. If in the first situation, nodular or, as it is sometimes called, tubercular leprosy is the result; if in the second, we have nerve or anæsthetic leprosy; if in both of these situations, then what is known as "mixed leprosy" is produced. These three forms of the completely developed disease, though having much in common,

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are, as a rule, clinically fairly distinguishable. It is customary, therefore, to describe them separately.

NODULAR LEPROSY.

This form of leprosy often appears without a well-marked preliminary macular stage, being ushered in, after a longer or shorter prodromal stage, by a smart attack of fever and the rapid development on

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Fig. 64.—Nodular leprosy. (*After Leloir.*)

the face or elsewhere of the specific lesion. In other instances a well-defined but, in comparison with nerve leprosy, short macular stage precedes the appearance of the characteristic lepromata (Fig. 64).

The essential element in nodular leprosy is the leproma. The dimensions, the combinations, the situations, the growth, and the decay of this give rise to the more manifest symptoms of the earlier stages, at all events, of the disease. The leproma, which will be more fully described in the section on

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the pathological anatomy of leprosy, is formed by infiltration of the deeper layers of the derma with what at first is a small-celled, somewhat dense neoplasm. As this slowly or more rapidly increases it forms a prominent, rounded boss or protuberance covered with unbroken epidermis. In size it ranges from the dimensions of a split pea, or of a bean, to a great plaque many inches across. In colour it differs according to its age and condition, and according to the natural hue of the skin of the leper; it varies from red to dirty pink in the earlier and congestive active stage, to dark brown or dirty yellow in the later stages. It is generally, though not always—especially at first, anæsthetic to some degree, if not absolutely so; it is devoid of hair, usually somewhat greasy-looking and, perhaps, stippled with gaping sebaceous follicles. Though not so hard as keloid growth, it is fairly firm to the touch, and, unless very extensive, can be readily raised up and freely moved over subjacent structures. Isolated lepromata are usually round or oval; when contiguous they may coalesce, forming patches of irregular outline.

When many lepromata run together, or are closely set, the growth causes the natural folds of the skin to be exaggerated; great disfigurement, especially of the face, may ensue. Thus the skin of the forehead and eyebrows—an early and favourite site of leprous infiltration—is thrown into massive folds and overhangs the eyes; the fleshy parts of the nose broaden out; the cheeks become massive; the lips are thickened and protrude; the chin is swollen and heavy; the external ears are thick and pendulous; and the bloated, dusky, wrinkled, greasy, passive countenance acquires the repulsive appearance very appropriately designated "leontiasis."

Nodules may appear in greater or less profusion on the limbs and body; favourite sites being the backs of the hands, the external surfaces of the arms, wrists, thighs, and the groins. On the trunk they may occupy very large areas, forming extensive plaques. As a rule, in the latter situation they are not so

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prominent as on the face and arms. The same remark applies to the legs, where the infiltration is usually dusky, diffuse, ill-defined, and prone to ulcerate.

From time to time, and at longer or shorter intervals, fresh lepromata appear, their formation generally concurring with an outburst of fever. Occasionally, and this is very often observed during an intercurrent attack of some acute disease —such as an exanthematous fever, or erysipelas, or even of some exhausting disease like phthisis—all or a proportion of the nodules are temporarily absorbed, leaving only slight traces behind. But the normal and usual fate of the nodule is either first to soften in the centre and then to be absorbed, leaving a smooth circular patch of scar tissue; or, after softening, to ulcerate and discharge a sticky, yellowish pus. This discharge tends to dry up into crusts, ulceration proceeding underneath. Finally the ulcer may heal, leaving an irregular, depressed scar.

When the septum of the nose is affected, the cartilage breaks down, the tip of the organ becomes depressed, and a stinking discharge escapes from the nostrils. In such circumstances breathing is very much interfered with, more especially if, at the same time, leprous deposit occurs or ulcerates in or about the glottis, the epiglottis, pharynx, tongue, or mouth generally. The senses of smell and taste are then lost for ever.

The eyes, also, are sooner or later attacked, lepromatous growth spreading from the conjunctiva on to the cornea or into the anterior chamber, or originating in the iris or ciliary body. Ultimately this organ also is destroyed.

Thus, in time, with the exception of that of hearing, one sense after another is lost. Ulcers form everywhere from the breaking-down of the nodules or from injuries to the insensitive skin. The cervical and inguinal glands, owing to leprous infiltration, swell and perhaps suppurate and become fistulous; the abdomen enlarges from leprous, perhaps combined with amyloid infiltration of the liver, and there may be diarrhœa from amyloid disease of the intestine. In addition to these troubles, if the patient

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live, the nerve trunks are attacked, and then the neuralgic, paretic and trophic lesions of nerve leprosy are superadded. The fingers and toes ulcerate and drop off, or they become distorted and atrophied; or the phalanges are absorbed, the hands and feet becoming reduced to useless stumps. A peculiar goat-like smell is emitted by the ulcerating, decaying body. Altogether, the blind, lame, unhappy wretch—still retaining his intellect, but devoid of every sense except that of hearing, breathing with difficulty through a stenosed larynx, and racked by neuralgic pains and irregular outbursts of fever—comes to present, before the inevitable death from exhaustion occurs, a sadder, more loathsome, and more repulsive picture than anything imagination could conceive. Fortunately, in a large proportion of cases, the leper is mercifully carried off by phthisis, pneumonia, or some intercurrent affection at an earlier period, and before his disease can be said to have run its full course.

NERVE LEPROSY.

Just as in nodular leprosy, in nerve leprosy the prodromal and macular stages may be severe, or slight, or altogether absent. Usually, however, in nerve leprosy, much more frequently than in nodular leprosy, the ulterior and more distinctive lesions are preluded by a long and well-marked macular stage, during which large areas of skin are occupied by erythematous (Fig. 65), by pigmented, or by vitiliginous patches. The ringed form of eruption is a very usual one; a red, congested, slightly elevated and, perhaps, hyperæsthetic border enclosing a larger or smaller area of pale anæsthetic, non-sweating integument—the whole resembling somewhat one of those extensive body-ringworms so common in natives of hot, damp climates, and for which these rings are sometimes mistaken. Such eruptions may come and go, or they may be permanent, or they may spread and multiply during many years before the more distinctive and graver signs of nerve leprosy are evolved.

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A frequent and very distinctive symptom of this type of the disease, occurring often about this time, is the sudden appearance of bullæ (pemphigus leprosus)—one or more or a series of them—on the hands, feet, knees, backs of thighs, or elsewhere. These bullæ vary in size from a pea to an egg. After a few days they rupture, exposing a reddish surface which presently crusts over, exfoliates, and finally turns into a pale, perhaps anæsthetic spot with a sharply defined, pigmented border. More rarely the site of the bulla ulcerates. Should similar bullæ be formed in the neighbourhood of the first, the resulting ulcerations may unite into an extensive, probably superficial, serpiginous-looking sore.

A time comes when evidence of profound implication of the nervous system, in the shape of severe neuralgic pains, formication, hyperæsthesia, or anæsthesia, becomes more accentuated. The lymphatic glands enlarge, and there is often considerable fever and general distress. Hitherto, the most prominent symptoms have been the skin lesions. These may remain or even increase; on the other hand, they may in part or entirely disappear. But whether the skin lesions increase or retrograde, evidences of profound implication of the peripheral nervous system now distinctly show themselves; the neuralgic pains still further increase, and hyperæsthesia, anæsthesia, and various paræsthesiæ, along with trophic changes in skin, muscle, and bone, the results of nerve destruction, become the dominating elements in the case.

If at this stage the ulnar nerve where it passes round the internal condyle of the humerus be examined, generally it will be found to be the seat of a fusiform swelling perhaps as thick as the little finger. Other nerves, such as the anterior tibial, the peroneal, more rarely the median, radial, brachial, and cervical nerves, especially where they pass over a bone and lie close under the skin, can be felt to be similarly swollen. Occasionally even the smaller nerves, where superficial, can also be detected hard and cord-like. At first these thickened nerves are tender on pressure, and the parts they supply may be the seats

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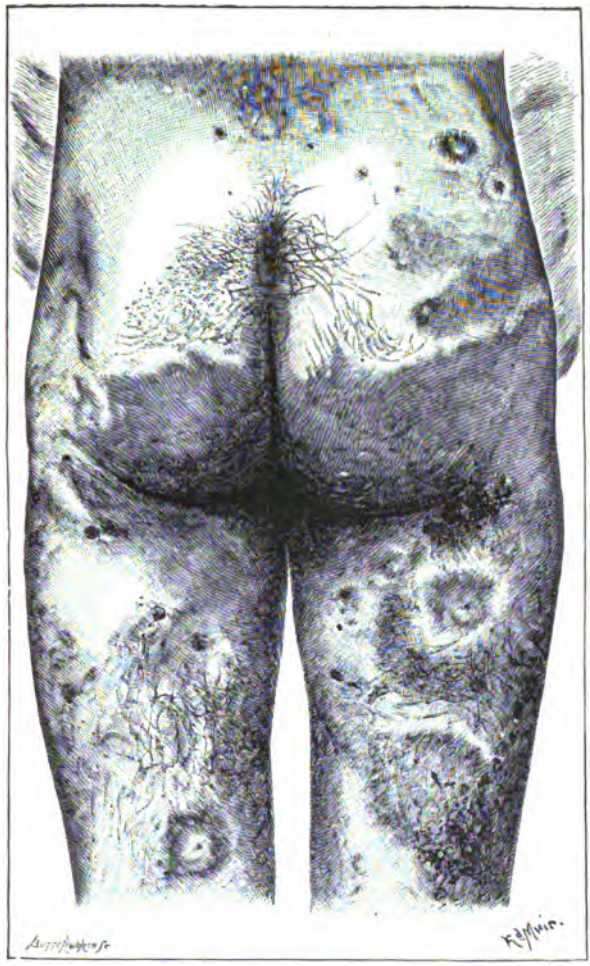

Fig. 65.—Nerve leprosy. (*After Leloir.*)

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of hyperæsthesia and acute neuralgia. By degrees the great thickening of the nerve trunks decreases somewhat, the hyperæsthesia and neuralgia subside, and anæsthesia, paresis, muscular atrophy, and other trophic changes take their place. For a time the condition may fluctuate; the neuritis apparently may come and go with corresponding changes in the condition of the area subserved by the affected nerves. Sooner or later, however, fibrotic changes ensue in the neural leprous deposits, and the nerve tubules ultimately atrophy and disappear. The nerve tissue is now irreparably damaged, and trophic changes steadily advance. In other instances anæsthesia comes on without neuralgic pains, without hyperæsthesia, without constitutional symptoms, without discoloration of the skin, the patient discovering its existence by accident.

In nerve leprosy the anæsthesia begins most commonly in the feet, the thighs, hands, arms, forearms, and face. Later, and more rarely, it affects the trunk. The anæsthesia, though associated with well-marked lesions of the larger nerves, does not always, or even as a rule, coincide accurately with the anatomical distribution of their terminals; a circumstance which tends to show that the anæsthesia is not always and simply the result of lesion of nerve trunks, but that it may be the effect of the destruction by the bacillus of the nerve terminals themselves; a suggestion which is strengthened by Gerlach's discovery that in anæsthetic leprosy the bacilli appear first in the skin around the nerve terminals, and only subsequently extend upwards to the nerve trunks. Another, and sometimes a very striking fact in nerve leprosy is the symmetry observed in the distribution of some of the anæsthetic areas. This symmetry is by no means invariable; in not a few cases, however, it is very perfect and remarkable.

At the outset the anæsthesia in the affected patches may not be absolute; it may also come and go; and it may be very superficial, deep pressure being for a long time appreciable. But when the

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anæsthesia becomes, as it were, settled in a part, it seems gradually to extend deeper into the tissues; so that after a time it is absolute, and the parts may be pinched, incised, and even seared with fire, and the leper be absolutely unconscious of pain or even of being touched.

Step by step with the progress of the anæsthesia, atrophy of the subjacent muscles supplied by the thickened nerves proceeds. Along with the atrophy there is a corresponding distortion and a corresponding loss of power. There is no ataxia or incoordination of movement—simply feebleness. Thus the forearm wastes, the grasp is weakened, the thenar and hypothenar eminences and the interossei melt

Fig. 66.—Nerve leprosy: main-en-griffe. (*After Leloir.*)

away, and the *main-en-griffe* or some such deformity is gradually produced (Fig. 66). Similar changes occur in the legs and feet, so that the power of walking is much impaired. The muscles of the thighs and upper arms, the pectorals, and the muscles of the face follow suit very much as in progressive muscular atrophy, only in the latter disease there is no superjacent anæsthesia.

In the affected nerve areas all the muscles are not simultaneously or equally attacked, so that, especially in the face, curious distortions may ensue. These facial atrophies, whether symmetrical or one-sided, in time produce a facies as characteristic of nerve leprosy as leontiasis is of nodular leprosy. Owing to muscular atrophy the eyes, after a time,

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cannot be closed; the upper lid droops, the lower lid becomes everted, and the eye itself may become fixed. At first, owing to exposure of the organ, there is lachrymation; but by-and-by the secretion of tears dries up, the congested conjunctiva becomes cornified, the cornea ulcerates or turns leucomatous, and in the end sight is entirely lost. Ulceration often occurs in the mucous membrane of the nose, the septum being destroyed as in the nodular form; the tip of the nose may then fall down or be entirely lost. The lips, too, may become paralysed, thereby interfering with articulation and permitting the saliva to dribble from the mouth in a constant stream. Changes occur, too, in the mucous membrane of the mouth; the gums may retract, exposing the maxillary bone, the teeth ultimately dropping out. Anæsthesia of the tongue and buccal mucous membrane, and implication of the muscles of mastication, may render eating and articulation very difficult.

In time the skin of anæsthetic patches on the limbs tends to atrophy; it loses its glands and hairs, and, in the end, may become so thinned and tense that it actually bursts into long cracks. The nails are not generally shed, but they become rough, or thinned, or atrophied into minute, hook-like appendages.

Ulcers form over exposed parts of the hands and feet. They may penetrate and disorganise the joints, and thus often cause fingers and toes to drop off, one after another. Or, perhaps, an abscess forms around a phalanx, destroys the periosteum, and ultimately leads to loss of the bone. Or a sort of dry gangrene may amputate finger or toe. Or there may be a curious interstitial absorption of one or more phalanges, the shaft of the phalanx wasting more rapidly than the articulating surfaces. In any of these ways the fingers and toes are distorted or destroyed. It is no unusual thing to see on a leper's hand a finger in which one or more of the phalanges have been thus got rid of without destruction of the fleshy part, or with only a general shrinking of this. Thus it comes about that a distorted, talon-like nail

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may crown a finger which is a mere stump; or, the finger having been entirely absorbed, the nail springs, as it were, directly from the knuckle.

Perforating ulcer of the sole of the foot, usually under the ball of the great toe or the heel, is a very common lesion in nerve leprosy.

On the whole, the advance of this form of leprosy is much slower than that of the nodular variety. The average duration of the latter is from eight to nine years, of nerve leprosy about eighteen years. Often such lepers live much longer—twenty, thirty, or even forty years. The end of these cases is quite as sad and repulsive as that of nodular leprosy. Death seldom results directly from the disease itself; diarrhœa, chronic nephritis, phthisis, pneumonia, or bronchitis being, one or other of them, usually the immediate cause of death.

MIXED LEPROSY.

As already explained, in most cases of nodular leprosy trophic changes from implication of nerve trunks ultimately supervene. Similarly, though not so frequently, nodular infiltration of the skin may appear in the course of what originally seemed to be a case of pure nerve leprosy. In yet other cases nodular and nerve lesions concur from the outset. In one or other of these ways what is known as mixed leprosy is produced. The lesions are in no way different from those already mentioned, and therefore this form of the disease does not call for more detailed description.

Pathological anatomy. — *Bacillus leprœ.* — The lesions of leprosy are the result, direct or indirect, of the proliferation of the *Bacillus leprœ* in the tissues. This parasite (Fig. 67) in size, shape, and staining reactions closely resembles the bacillus of tubercle. In length it is from half to two-thirds, and in breadth about one-sixteenth the diameter, of a blood corpuscle. The ends of the rod—which is always straight—are in many specimens somewhat attenuated; and in many instances—presumably in old bacilli—a moniliform arrangement of the proto-

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plasm, as if from spore formation or, according to Hansen, from disintegration, can be detected. By some authorities it is said to possess a gelatinous capsule. In common with *Bacillus tuberculosis* and *Bacillus smegmæ* it retains carbol-fuchsin stains after being treated with mineral acids. It may be distinguished from *Bacillus tuberculosis* by its staining more readily with cold weak solution of carbol fuchsin, and by being decolorised more easily with dilute acids; by the impossibility hitherto experienced of growing

Fig. 67.—Bacillus lepræ. (× 1000.) (*Muir and Ritchie.*)

it on the usual culture media, and of successfully inoculating it into man and the lower animals; by its tendency to occur in dense clusters and in greater numbers; and by its very generally being found inside cells or, according to Unna, in zooglœa masses in the lymphatic spaces.

Specimens of the bacillus can be procured readily by excising a portion of a leproma—a proceeding, in consequence of the absence of sensation in most tubercles, not usually much objected to by lepers; or they may be obtained by including a succulent leproma in a pile clamp, slowly screwing up the jaws

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of the instrument so as to drive out the blood, pricking the now pallid leproma, and then collecting on a cover-glass the droplet of "leper juice" which exudes from the puncture. The juice may be spread out on the cover-glass, fixed, stained, and decolorised as for the demonstration of tubercle bacilli; or it may be examined fresh. Better preparations are obtained by making with a small scalpel a minute incision into the compressed leproma, scraping some of the tissues from the under surface of the skin, and smearing this with the juice on to the cover-glass. One must be careful to exclude the possibility of contamination with *Bacillus tuberculosis*, with which lepers are often infected.

If examined fresh, or if a morsel of leproma be teased up in water, the bacilli may be seen both inside and outside the cells and in active motion. Whether this motion is simply molecular, or whether it is vital, is hard to say; probably the former, for, whilst osmic acid does not stop it, it is immediately arrested by the addition of viscid fluids, such as glycerine or albumin water.

The bacillus is found in all primary leprous deposits; in the skin leproma—where it occurs in prodigious numbers; in the meagre infiltration of the macular eruptions—where it is much more sparsely distributed; in the early stage of leprous neuritis—where, also, it is present only in small numbers; in the specific lesions of the liver, spleen, testes, and lymphatic glands. In the blood-vessels it has been found in the endothelium and, occasionally, free in the blood or enclosed in leucocytes. It is abundant in the purulent discharges from the nose, from ulcerating lepromata or other forms of primary leprous infiltration. It has very rarely been found in the spinal cord or in the lungs. It is doubtful if it occurs in the brain, the intestinal tract, or in the kidneys, although the latter are prone to inflammation in leprosy. It is not found in muscle, in bone, or in cartilage; and it is not necessarily present in the secondary trophic lesions of nerve leprosy, or in secondary inflammatory effusions.

Many unsuccessful attempts have been made to

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cultivate the lepra bacillus. Success has recently been claimed by Spronck, Van Houtum, and Carasquilla. The two former used fish bouillon as a culture medium; the latter, meat broth. Spronck's bacillus, which had some morphological resemblance to Hansen's bacillus, but differed from it in staining reactions, agglutinated with leper serum. Van Houtum's bacillus clumped less markedly in leper than in non-leper serum, but in leper serum the Pfeiffer-Bordet reaction was much more distinct with leper than with non-leper serum. Van Houtum's bacillus differed morphologically and in staining reaction from Hansen's bacillus. Carasquilla's bacillus resembled Hansen's morphologically and in staining. He injected filtered cultures into horses, and claims to have obtained encouraging curative effects from the serum of horses so treated. More recently Rost claims to have succeeded in cultivating the bacillus in broths from which the sodium chloride had been removed.

The leproma.—The young leproma presents a smooth, white, glistening section. When the leproma is older the cut surface has a brown tint, and the morbid tissue may become, from fibrotic changes, harder, or, from degeneration, softer. The specific lesion of leprosy differs from that of tubercle inasmuch as the former is well supplied with blood-vessels, contains no true giant cells and never undergoes caseation. If hardened, cut, stained, decolorised, and examined under the microscope, the leproma is found to consist principally of small round cells about the size of a leucocyte, epithelioid cells, and fusiform cells—the two latter in increasing numbers with the age of the leproma. It can be seen that these cells have infiltrated and partially dissociated all but the most superficial layer of the derma. It may be further observed that the cells are arranged for the most part in groups, generally around and near blood-vessels; and that a very large proportion of them contain bacilli, some cells having only a few, whilst others are literally crammed with the organisms. Isolated bacilli are also found scattered through the prepara-

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tion, apparently free in the lymph spaces. The bacilli are never seen inside the nuclei of the implicated cells.

In addition to the bacilli-bearing cells, and increasing in number with the age of the lesion, a number of brown granular bodies, larger and smaller, which have been named "globi," are to be found. These Hansen holds to be cells in which the bacilli have perished and become granular. It is to them that the brown colour of old lepromata is due.

There has been considerable discussion as to the exact position of the bacilli as regards the lepra cells —whether they lie inside the cells or whether they are free. On the one hand, Unna holds that they lie free in the lymph spaces, and that they are never in the cells, the appearance of cell inclusion being produced by the zooglœa arrangement so common with bacteria. On the other hand, Leloir maintains that some of the bacilli are free, whilst others are inside the cells. A third set of observers, following Hansen, hold that the bacilli are almost invariably included within cells, the nuclei of which can readily be demonstrated surrounded by the parasites.

Other lesions.—The histology of the infiltrated macula is practically the same as that of the leproma, the number of bacilli, lepra cells, and globi being proportionately fewer. In old maculæ, as in very old lepromata, the bacilli may be hard to find or entirely absent. In the anæsthetic maculæ the terminal nerve fibres are degenerated.

As the fusiform thickening of the larger nerve trunks in nerve leprosy is a secondary inflammation, bacilli may not always be found in it, although at the very commencement of the nerve disease bacilli, both in cells and, according to Leloir, free between the nerve tubules, are present and may even lie in the nerve tubules themselves. In time the affected nerves become mere fibrous cords destitute of nerve tubules.

The anatomy and histology of the various trophic lesions are such as are found in other examples of destructive neuritis, and are in no way peculiar to leprosy; they do not, therefore, call for description here.

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In nodular leprosy the liver and spleen are the seat, in many instances, of a peculiar infiltration which, in well-marked examples, may be visible to the naked eye. Fine yellowish-white dots and streaks are seen to occur in the acini of the former. These dots and streaks consist of new growth in which bacilli abound. According to Leloir, the parasites are never found in the hepatic cells themselves.

In all cases of nodular leprosy the testes atrophy and undergo fibrotic changes, bacilli and globi being found both in and around the tubules, free and in cells.

In all forms of leprosy the lymphatic glands appertaining to parts in which leprous deposit is present are characteristically affected. They are swollen and hard, and on section the gland tissue is seen to have a yellowish tinge from an infiltration which contains numerous bacilli and globi.

Albuminoid disease of the alimentary canal, liver, and spleen, and nephritis occur in a large proportion of the cases of nodular leprosy.

Diagnosis.—The touchstone in all doubtful cases is the presence or absence of anæsthesia in some skin lesion, or in some skin area. Anæsthesia is rarely absent in leprosy; generally, in the implicated spots it is complete, or nearly so. It should be particularly sought for towards the centre of maculæ, in the pale patches left after the fading of former maculæ, in the hands and feet, and in nodules of some standing. In no other skin disease is definite anæsthesia a symptom.

Vitiligo or leucodermia—sometimes called white leprosy, and by the vulgar very generally regarded as true leprosy—bears a certain resemblance to the pale post-macular patches referred to; not to mention other features, the absence of anæsthesia in leucodermia at once settles diagnosis.

Further assistance may sometimes be got in doubtful cases from the fact that leprous spots rarely perspire. A hypodermic injection of pilocarpine is of use in bringing out this point.

The sensory and trophic lesions of syringo-myelia might be mistaken for nerve leprosy, but the general

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history of the case, the history or presence of macular eruption, of thickened nerve trunks, and of enlarged lymphatic glands in leprosy, and their absence in syringo-myelia, are mostly sufficient to establish a diagnosis.

It is hardly necessary to point out the diagnostic marks of leprosy as against syphilis, erythema multiforme, erythema nodosum, trypanosomiasis, lupus vulgaris, lupus erythematosus, psoriasis, eczema, lichen planus, cheloid, body-ringworm, erythrasma, pityriasis versicolor, pellagra, elephantiasis arabum, etc. Mistakes can scarcely be made unless from carelessness, or by someone completely ignorant of the nature, history, and symptoms of these diseases.

In approaching the diagnosis of skin eruptions, localised pareses, muscular atrophies, and anæsthesia in patients living in or coming from a country in which leprosy is endemic, the possibility of their being attributable to this disease must be borne in mind. If doubt exist, and it be found feasible, search for the bacillus should be made in eruptions, or in thickened nerves, or in any nasal or other morbid discharge that may be present. If this be found the diagnosis of leprosy will be infallibly established.

Prognosis.—Complete recovery is an event so rare in leprosy that, though it may be hoped for, it must not be expected. Recovery from the actual disease itself—that is, in the sense that fresh leprous infiltration may cease to occur, and old infiltration may be absorbed, and that the bacilli may die out—is perhaps the rule in nerve leprosy ; but the effects of the leprous process are generally permanent, the trophic lesions resulting from nerve destruction being irremediable. Such cases may live, however, for many years—thirty or forty—and die of some other disease.

Nodular leprosy is usually a much more acute disease than nerve leprosy, sapping the strength and general health much more effectually and more quickly. It rarely runs its full course, death being brought about by some intercurrent disease, such as, and especially, phthisis, nephritis, albuminoid degeneration of the alimentary tract, dysentery, stenosis of the larynx,

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and pneumonia. It may even prove fatal as a sort of "galloping" leprosy within a year of its first declaring itself.

Ætiology.—*Age.*—It is open to question if leprosy has ever been seen in the fœtus. It has once or twice been reported in the newly-born. Cases are also on record of its occurrence as early as the first and second years of life; such cases, however, are quite exceptional. Leprosy is extremely rare before the fifth or sixth year. In the great majority of instances the disease begins between the tenth and thirtieth year. It rarely commences after forty, although it has been known to begin up to and even after seventy.

Sex; occupation; social and hygienic conditions.—Apart from social conditions as affording opportunity for contagion, sex seems to have little bearing on the liability to leprosy. The same may be said of occupation, and social and hygienic conditions in general. Very probably bad food and bad hygienic circumstances have in this, as in most germ diseases, a predisposing influence; but they certainly cannot create a lepra bacillus and leprosy, any more than they can create an acarus and itch. This is abundantly shown by the absence of leprosy at an earlier period in countries in which, without alteration in the food or other hygienic conditions, the susceptibility of the natives to the disease was subsequently proved by its rapid spread on being introduced from without, *e.g.* the Sandwich Islands and New Caledonia; and, also, by the disappearance of the disease, in other instances, under the influence of the segregation and isolation of lepers, without any concurrent material alteration in food or other circumstances, *e.g.* Scotland, Ireland, and most European countries.

Sir Jonathan Hutchinson very sagaciously and truly remarks that leprosy is more especially a disease of semi-civilisation. Savages are exempt; the highly civilised are exempt; but when the savage begins to wear clothes and live in houses he becomes subject to the disease. In other words, in the early

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stages of civilisation, opportunities of infection are multiplied, and their influence is not counteracted by cleanliness of house or person.

Climate.—Climate can in no way be considered a cause of leprosy, for leprosy exists in all climates and in all latitudes. But it does seem to have some influence in determining, to a certain extent, the type the disease assumes. It would appear that the nodular form is more common in cold, damp climates; the nerve form in warm or dry climates.

The lepra bacillus.—Hansen remarks, "There is hardly anything on earth, or between it and heaven, which has not been regarded as the cause of leprosy." However true this remark may be as regards times prior to Hansen's discovery, we are now practically certain that the lepra bacillus is the cause of leprosy. The only gap in the evidence, otherwise conclusive, lies in our present inability to convey, by inoculation or otherwise, the cultivated bacillus to the lower animals, or, perhaps, to man himself.

Many attempts have been made to communicate leprosy to man by inoculation; hitherto, with one questionable exception, all have failed. A Sandwich Islander, apparently at the time free from leprosy, was inoculated from a lepra nodule. Within a month he had symptoms of leprous neuritis; two years later he was a confirmed leper; and in six years from the date of the inoculation he died of leprosy. Unfortunately, the subject of the experiment was a native of a country in which leprosy was extensively endemic, and, besides, he had lived among lepers; in fact, members of his family were lepers. However possible it may be that the bacillus in this instance had been communicated by the inoculation, the circumstances in which the experiment was made, and the unusual shortness of the incubation period, are against its being regarded as conclusive evidence of the inoculability of the disease.

To bridge over this important gap in the evidence, we have to fall back on the close analogy that subsists between *Bacillus leprœ* and *Bacillus tuberculosis*, the leproma and the tubercle, leprosy and

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tuberculosis. In consideration of this and other circumstances, it is generally conceded that *Bacillus leprœ* is the cause of leprosy, just as *Bacillus tuberculosis* is the cause of tubercle. Authorities differ, however, as to the way in which the bacillus is acquired.

How acquired.—It is absurd to suppose that an organism, no matter how humble its place in the scale of life, can originate *de novo*. Disregarding this, we have to consider two principal views as to the way in which the bacillus is acquired—heredity and contagion.

Heredity.—From the fact that it tends to run in families and that in certain instances it assumes the appearance of atavism, leprosy, until the *Bacillus leprœ* was discovered, was almost universally—as it still is by some—believed to be an hereditary disease. That this belief, in the same sense as that tubercle may be said to be hereditary, was well founded is quite possible; that is to say, that certain physio-pathological qualities predisposing to leprosy may be inherited. But since the discovery of the bacillus it is impossible any longer, if we properly consider it, to believe that the bacillus itself, and therefore the disease it causes, can be hereditary in the scientific sense of the word "hereditary." Physiological peculiarities and susceptibilities may, but parasites cannot, be inherited. It is true the ovum may be infected by a germ, as in syphilis; but infection is not heredity. That the ovum can be infected at some stage of its existence by the lepra bacillus is proved if it be true that children have been born with the lesions of leprosy on them. But the fact that leprosy is common in the descendants and blood collaterals of lepers is no proof of ovum infection in every, or perhaps in any case; for family liability is quite as explicable by an hypothesis of contagion, or outside infection, as by an hypothesis of inherited infection. Not only may the individuals of a family inherit a family predisposition of susceptibility to the bacillus, but, as a family, the members of it are generally at one time or another closely associated, exposed to the same hygienic influences, liable by contact to communicate each other's parasites, or to acquire the parasites latent in their common surroundings. Because the members of a family simultaneously, or one after another, contract scabies, or ringworm, or typhoid, no one supposes on this account that any of these diseases is hereditary.

Without absolutely denying the possibility of ovum infection, the probability is that such an event is very rare. The age at which leprosy usually appears is against such a supposition. The latency of a germ for twenty, thirty, forty, or even seventy years is an extremely improbable thing and

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without parallel in pathology. Atavism, or rather, the appearance of atavism, frequently met with in leprosy, is also against such a supposition; for, although we can understand infection of an ovum by a leper parent, we cannot understand the transmission of a germ from a grandparent to a grandchild through a parent who is not, never was, and may never become a leper. Such a thing would imply proliferation of the bacillus in the parent without pathological evidence of its presence.

Even admitting that leprosy is sometimes transmitted by ovum infection, this method of transmission cannot be the only one, or even a common one, for many lepers have no leper ancestors; and, as is well known, the healthy European, coming from a country in which leprosy has not been seen for generations, may acquire leprosy on visiting a country in which the disease is endemic.

If leprosy be communicated generally, or even sometimes, by parent to child by heredity, how explain the striking fact, brought out by Hansen, that of the numerous offspring of 160 Norwegian lepers who emigrated to America not one has become a leper? Or, again, the equally well attested fact that children sometimes become lepers first, their parents afterwards.

Another powerful argument against the doctrine of heredity is the circumstance that lepers become sterile early in the disease. From this it is evident that unless the ranks of leprosy are recruited in some other way than by heredity the disease would inevitably die out in one, or at most two generations.

From considerations such as these the view that leprosy is an hereditary disease has now few adherents among the well informed.

Contagion.—With few exceptions, the best authorities believe that leprosy is propagated by contagion, and only by contagion. The same unanimity of opinion does not obtain as to the particular way in which, or medium by which, the contagium is applied; but that it passes directly or indirectly from the infecting leper to the infected, nearly all are agreed to regard as being practically proved. The principal facts and considerations on which this important conclusion is founded are as follows:—

Leprosy is a germ disease, and therefore it cannot originate *de novo*. It must come from a pre-existing germ whose habitat may be air, soil, water, plant, beast, food, or man. That the habitat of the infecting germ is man is rendered in the highest degree probable by the fact that the germ is found in the human tissues and hitherto nowhere else; and by the

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fact that leprosy has never been known to appear on virgin soil independently of the prior advent of a leper. When a leper settles down in virgin country, after a time cases of the disease crop up among his companions and immediate neighbours. Some of these newly-made lepers, proceeding to a different part of the country, in time become centres for other groups of cases. Thus in the early history of the introduction of leprosy into a virgin country—as New Caledonia — the spread of the disease from individual to individual, and from place to place, can be, and has been, traced.

In further proof it can be advanced that not only may a native of a non-leper country acquire the disease on visiting a leper country, but he may also communicate the disease to others, his countrymen, on his return to his own country. There is at least one well-authenticated example of this on record. Dr. Hawtrey Benson, in 1872, showed at the Medical Society of Dublin a leper, an Irishman, who had acquired his disease in the West Indies. After his return to Ireland he slept in the same bed as his brother, who, moreover, sometimes wore the leper's clothes. In time the brother, who had never been out of the United Kingdom, became a leper, and was shown to the same medical society in 1877. In this case there can be no question of fact or of diagnosis. Such a case can only be explained by contagion. Though not quite so well authenticated and conclusive, many similar instances of the communication of leprosy by contagion are on record. The case just mentioned is alone almost conclusive; for if leprosy is proved to be communicable by contagion in one case, the probabilities are that it is so acquired in every case.

It has been advanced against the contagiousness of leprosy, that it attacks a very small proportion only of the attendants, nurses, and doctors in leper asylums. But might not a similar objection be raised to the contagiousness of scabies or of ringworm? The conditions for successful contagion are known and can be easily avoided in the latter diseases; they are

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not known, and are therefore not invariably avoided in leprosy. All contagious diseases demand certain conditions for their diffusion. In some diseases these conditions are easily complied with and often concur; in other diseases they are with difficulty complied with and rarely concur. Leprosy belongs to the latter category.

Probably intimate personal contact, and certain concurrences in the phases of the disease with special conditions in the health or physiological state of the recipient, are necessary for the successful communication and acquisition of leprosy. The simple implantation of the bacillus does not suffice; for, as already pointed out, of the many inoculations that have been made only one has any claim to be regarded as having been successful.

Articles of diet—such as imperfectly cured fish—have been incriminated as media for infection. Sir Jonathan Hutchinson has for many years strenuously advocated this doctrine. The historical, epidemiological and circumstantial evidence on which it is sought to establish this speculation, though highly suggestive, is in the opinion of most authorities insufficient.

Prevention.—If it be conceded that leprosy is caused by a germ, that it is contagious directly or indirectly, and that it never breaks fresh ground unless first introduced from without and by a leper, then the leper must be regarded as a source of danger, and, *quâ* leprosy, the only source of danger to any community he may live amongst. Therefore a sure, and the most effectual way of suppressing the disease is the thorough isolation of existing lepers. There are many difficulties, however, especially in such countries as India, in giving practical expression to what appears to be a perfectly logical conclusion—difficulties springing from the rights of the individual, finance difficulties, difficulties arising from concealment or incorrect diagnosis, as well as from the continued introduction of fresh cases from without. These and other obvious obstacles, incident to any attempt at a wholesale system of thorough isolation, are so great

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that the most that can be hoped for at the present time, and in the present state of public opinion, is some modified system of segregation and isolation, such as has worked so successfully in recent years in Norway.

Where possible, therefore, lepers should be segregated in isolated asylums, which should be so conducted as to prove attractive. Those who cannot be made, or persuaded, to enter these asylums should be isolated as much as possible from their families and the public; scrupulous cleanliness of their persons and houses should also be insisted on. Lepers ought not to be allowed to beg in the streets—as is often the case in Eastern cities, to keep shops, or to handle food or clothes intended for sale, to wander about the country as pedlars or mendicants, to hire themselves out as servants or prostitutes, or to frequent fairs and public places. All lepers in the ulcerative stage of the disease, when it is to be presumed that myriads of bacilli are being constantly given off from their sores, should be still more scrupulously isolated, their discharges, clothes, and dressings being systematically destroyed or disinfected. A child born of a leper should at once be removed from the diseased parent, and, if necessary, cared for at the public expense.

Leprosy is feebly contagious, or rather, the conditions for successful contagion rarely recur; so rarely, that it is more than probable that under such a modified system of segregation and isolation as that indicated, they would recur so seldom that the disease would rapidly die out.

Vaccination.—It has not been actually proved that leprosy can be communicated by vaccination, although there is some evidence in favour of such a supposition. But, although this has not been proved, it is an obvious and very desirable precaution, in countries in which the disease is endemic, to take care that the vaccinifer is not only not the subject of actual leprous eruption, but, also, that he or she comes from a family and community free from leprosy. An apparently healthy vaccinifer may contain lepra bacilli in a latent state; may be, in fact, a potential leper and capable of communicating the disease.

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Treatment.—Scrupulous and systematic attention to personal and domestic hygiene and cleanliness; frequent bathing and the free use of soap; frequent changes of underclothing; good food; fresh air; light work; the avoidance of over-strain, fatigue, and of exposure to bad weather; these things are all of prime importance in the treatment of leprosy, and should be insisted on. It has been found that most lepers on being placed in favourable hygienic conditions improve for a time, and that in a small proportion of cases the disease by these means may sometimes be actually arrested. Europeans who have contracted leprosy in the tropics almost invariably undergo temporary improvement on return to the more bracing climate and more nutritious diet of their native lands. It seems to me that the methods of treatment now coming into vogue for tuberculosis are equally applicable to leprosy.

Many drugs have been regarded, from time to time, as being more or less in the nature of specifics in the treatment of this disease. But, though some of these drugs appear for a time to do good, and in consequence acquire a certain degree of popularity, hitherto all of them, one after another, have sooner or later fallen into disfavour. One is very apt to be deceived in estimating the value of a drug in leprosy. The leper applies for treatment generally during, or soon after, one of the periodical exacerbations of the disease, and when the nodules and other eruptions are active and well pronounced. In the natural course of events, and without treatment of any description, especially if the patient be placed under favourable hygienic conditions, these acute manifestations tend to become quiescent, and the disease temporarily to ameliorate. Observers are too apt to attribute this natural and temporary amelioration to whatever drug the patient may happen to be given at the time. Moreover, in judging of the value of any drug in leprosy, it must be remembered that the disease may be arrested spontaneously, or even be recovered from, without the use of any drug whatever.

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Chaulmoogra oil (*Oleum gynocardium*), in doses of from two to ten up to forty drops or more, according to tolerance, three times a day, together with inunction of the same drug mixed with some oil, is a favourite remedy with English practitioners. Such lepers as can assimilate large doses of this drug appear to derive benefit. Sandwith has reported a case in which marked benefit followed persistent hypodermic administration of chaulmoogra. I have had lepers under my care who, in addition to large doses of chaulmoogra by the mouth, received hypodermic injections daily up to one drachm of the drug. The improvement for a time was marked. The bacilli, however, were just as abundant in the nodules during and after as before treatment, and there was no alteration in their appearance. Encouraged by the clinical results, I have persevered with this treatment for many weeks at a time. In one instance the patient died from what was suspiciously like fat embolism; in another, while very large doses of chaulmoogra were being taken by the mouth and injected hypodermically, severe leprotic fever, associated with profuse eruption of lepromata, set in.

Gurjun oil, once in favour, seems to have been abandoned.

Unna claims to have cured several cases of leprosy by the internal administration of ichthyol in increasing doses, combining the internal medication with vigorous rubbing of the arms and legs twice a day with pyrogallic acid (10 per cent.) in lanolin, and the cheeks and trunk with chrysophanic acid (10 per cent.) in lanolin; at the same time applying to the forehead and chin a plaster of chrysophanic and salicylic acids with creosote, changing the plaster every day. The treatment is continued for a month, and is then followed by a course of warm baths before being resumed.

Tuberculin has also been tried. It produces a local and a general reaction, which is sometimes curiously delayed for one or two days. So far from doing good it seems to aggravate the disease, causing

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fresh eruptions, and, also, causing bacilli to appear in the blood.

Dr. Radcliffe Crocker has recorded several cases of leprosy in which great improvement followed weekly hypodermic injections of one-fifth of a grain of perchloride of mercury.

Iodide of potassium aggravates leprosy if given in full doses; it not only affects the general health prejudicially, but it causes fresh eruptions to appear.

Danielssen regards salicylate of soda, combined with cod-liver oil, quinine and iron, good food, and good hygiene, as the best treatment for leprosy. He claims for the salicylate, if commenced within the first few months from the appearance of the disease, that it sometimes effects a cure. He begins with fifteen grains, four times a day, and gradually increases the dose during six months or a year.

I have tried thyroidin in a case of nerve leprosy. The patient is now absolutely free from symptoms.

Hydroxylamin, europhen, naphthol, salol, methylene blue, and aristol have also been tried recently; the results have not proved encouraging.

It has been proposed to treat leprosy by inoculations of the erysipelas streptococcus, or by injections of the filtered toxin obtained from cultures of that organism (Impey).

Nerve stretching, with or without nerve splitting, has been strongly advocated (McLeod) for the cure of leprous neuralgia, anæsthesia, muscular atrophy, and other trophic lesions. At the best they can benefit the local lesion alone, and that but temporarily, and only in the earlier stages of the leprous neuritis before the nerve has undergone fibrous transformation.

In the case of leprous nodules spreading on to the cornea and threatening to interfere with the line of vision, Brockmann has shown that the extension of the leproma may be arrested by division of the cornea on the pupillary side of the lesion; it is found that the bacilli do not traverse the cicatrix. Tarsorrhaphy for ectropion of the lower lid; iridectomy for iritis, or synechiæ; tracheotomy for laryngeal stenosis;

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and necrotomy for bone disease, may sometimes have to be performed. Horder strongly recommends amputation for perforating or other forms of ulceration; the general health is much improved by the removal of such sources of sepsis. The existence of leprosy does not materially interfere with the success of surgical operations. I once removed an enormous elephantiasis of the scrotum from a confirmed leper; the presence of the leprosy did not prevent sound healing of the extensive operation wound, the man making a good recovery so far as the operation was concerned.

If only one tubercle, or one limited lepra macula is present, and there have been no constitutional signs of a general invasion, it is advisable to excise freely the affected spot.

What promises to prove an important advance in the therapeutics of leprosy has been introduced recently by Prof. Deycke under the name of Nastin Treatment.

Professor Deycke obtained from a case of nodular leprosy a peculiar acid-fast bacterium—*Streptothrix leproides*—resembling in many respects *Bacillus leprœ*, but differing from the latter inasmuch as it could be readily cultivated. In unskimmed milk it forms a brilliant orange-red pellicle, which on digestion with ether yields a fatty substance—"Nastin"—of definite chemical character. Injections of pure nastin in oily solution give rise in some lepers to inflammatory reaction of varying degrees of intensity—it may be violent; in other lepers again no such reaction occurs. Concurrently with reaction there is pronounced bacteriolysis and disappearance of the lepra bacilli as evidenced by their losing their staining reaction and disintegration. Several patients treated in this way improved, some apparently recovering; but the uncertainty as to whether in any given case reaction might not prove of so violent a character as to be dangerous to life imposed limitations to its general use.

Finding that benzoyl-chloride ($C_6H_5—CO—C$), by removing their fatty protective contents, rapidly

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deprived tubercle bacilli of their "acid-fastness," he concluded that this substance might act similarly on the lepra bacillus, and also finding that benzoyl-chloride was innocuous, he concluded that by combining it with nastin the therapeutic efficiency of the latter might be so reinforced that it could be used in doses so small that violent reaction would be avoided. Experiment justified the conjecture, and although benzoyl-chloride administered alone has no therapeutic action in leprosy, given in appropriate combination with nastin in a large proportion of instances, although not in all, the results are highly satisfactory, the lepra bacilli and lepra lesions slowly or more rapidly disappearing.

Prof. Deycke's hypothesis as to the mode of action of the combination is to the effect that the nastin element, having affinities with the fat of the lepra bacillus, acts merely as the introducer of the benzoyl-chloride, which is the actual bactericide.

As the result of much experience Prof. Deycke considers that what he calls "Nastin B^1," in which one part of nastin is dissolved in forty parts of benzoyl-chloride, and this again in sterile olive oil, is the best combination, rarely, if properly administered, giving rise to reaction. A weaker solution, "Nastin B^0," he uses in cases of ophthalmic and nerve leprosy, as a special precaution against dangerous reaction. After the weaker preparations have been used for some time a stronger nastin, B^2, may be employed.

There are certain points in the nastin treatment of leprosy on which Prof. Deycke lays stress. (1) Reaction from excessive doses is unnecessary and should be avoided. (2) Not too frequent injections; once a week suffices. (3) Perseverance for months and years, intermitting the injections for a month or two occasionally.

Reports from British Guiana, where systematic trial of this treatment on a large scale has recently been carried out, speak most favourably of the results, as do others from India and New Zealand.*

* Nastin preparations may be obtained from Messrs. A. & M. Zimmermann, 3, Lloyd's Avenue, London, E.C.

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CHAPTER XXXVI

YAWS (FRAMBŒSIA)

Definition.—Yaws is a contagious, inoculable disease characterised by an indefinite incubation period followed usually by fever, by rheumatic-like pains, and by the appearance of papules which generally develop into a fungating, encrusted, granulomatous, eruption. It runs a chronic course; is mostly protective against a second attack; and, to a certain extent, is influenced by mercury and potassium iodide.

Geographical distribution.—Yaws is widely diffused throughout the greater part of the tropical world. In certain places it is very common—as in tropical Africa, particularly on the west coast; in many of the West India islands; in Ceylon, where it is one of perhaps several diseases included under the term *Parangi;* in Fiji, where it is known as *Coko;* in Java; in Samoa; and in many of the islands of the Pacific. It is difficult to say to what extent it exists in India; some deny its presence there altogether, but recent observations show that it does occur there to a limited extent. Powell has recognised and described it as occurring in Assam. Barker and Gimlette have recently shown that the skin disease described by Brown under the name of *Purru*, and common in parts of the Malay peninsula, is yaws. Yaws occurs in China, but is rare there—at all events on the coast. In some of the West India islands, and in Fiji, almost every child passes through an attack. In the latter, according to Daniels, those children who do not acquire the disease in the ordinary way are inoculated with it by their parents, who regard an attack of yaws as an occurrence more or less necessary and wholesome. Nicholls has made a careful and admirable study of West Indian yaws. His inclination is to look upon

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parangi, coko, and similar Asiatic and Pacific island diseases as specifically different from the African and West Indian disease. Daniels, however—a most accurate observer, who has had extensive experience in Fiji, in British Guiana, and in Africa—shows very clearly that in these places the diseases are identical. Probably the view that certain forms of the parangi of Ceylon are not yaws is likewise incorrect.

It is impossible at the present day to settle the point, but it seems probable that yaws was originally an African disease, and, so far as America and the West Indies are concerned, that it was introduced by negro slaves. In the days of West Indian slavery the specific and infectious nature of yaws was thoroughly recognised. The planters, from commercial, apart from other considerations, by instituting yaws-houses and similar repressive measures, took much trouble to keep the disease under. Since emancipation has permitted the West Indian negro to revert to some extent to the state of savagery from which he had partly emerged, yaws has again become very prevalent, and is now a principal and loathsome feature in the morbidity of these islands.

Ætiology.—*Contagion and heredity.*—As yaws is highly contagious, all circumstances favouring contact with the subject of the disease favour its occurrence. Simple skin contact does not suffice; a breach of surface is necessary. Probably the virus is often conveyed by insect bites, or by insects acting as go-betweens and carrying it from a yaw sore to an ordinary ulcer. Thus the disease often commences in a pre-existing ulcer. Cases are prone to originate in certain dirty houses, the virus from previous yaws patients seemingly impregnating the floors and walls of the filthy huts in which the latter had resided. In this way the disease may be acquired without direct transference from an existing case.

Yaws is neither hereditary nor congenital. A pregnant mother suffering from yaws does not give birth to a child suffering from the same disease, nor one which will subsequently develop yaws unless the

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virus be first introduced directly through a breach of surface after birth. It is not conveyed by the milk; nor does a suckling suffering from yaws necessarily infect its nurse.

Age, sex, occupation, race.—Although two-thirds of the cases in the West Indies occur before puberty, no age is exempt. Three males are infected to every female attacked. Occupation has no manifest influence. In the West Indies, Europeans, Chinese, and Indians catch the disease if exposed to the contagium.

The virus.—Both Pierez and Nicholls found a micrococcus in yaws tissue and in the exudation. Cultures of this micro-organism introduced into certain animals did not give rise to the disease.

Recently (Feb. 1905), by overstaining with Leishman's and Giemsa's stains, Castellani has demonstrated in scrapings of yaws tissues the presence of an extremely delicate spirochæte, *Spirochæta pertenuis* (*S. pallidula*), very like that of syphilis. Castellani's observations are confirmed by Wellman, Powell and Borne. He remarks that in a very small proportion of the spirochætes there is an ovoid expansion at one end, rarely in the continuity of the filament.

Symptoms.—*The initial fever.*—In yaws there is an incubation stage of very variable duration—two weeks to six months*—the appearance of the characteristic eruptions being preceded by a certain amount of constitutional disturbance. The intensity of the general symptoms varies within wide limits. Sometimes they are hardly perceptible, and are not complained of; usually there is well-marked malaise with rheumatic pains. Occasionally there is severe constitutional disturbance, lasting for about a week, with rigor, smart fever—100° to 103°—persistent headache, pains—worse at night—in the long bones, joints, and loins, and sometimes gastric disturbance and

* Paulet, who inoculated fourteen healthy persons with yaws, found the first lesion in from twelve to twenty days; Charlouis, in twenty-eight inoculations, observed a papule at the site of inoculation after fourteen days. Naturally acquired yaws is reputed to have a longer incubation period than the inoculated disease.

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diarrhœa. During the decline of these constitutiona symptoms the eruption appears.

Stage of furfuraceous desquamation.—The skin becomes harsh and dry, loses its natural gloss, and here and there patches of light-coloured, very fine furfuraceous desquamation, best appreciated with the aid of a lens, are formed. These patches are mostly small and circular; occasionally they are oval, irregular, or form rings encircling islets of healthy skin. Their extent and number are very uncertain. They

Fig. 68.—Case of Yaws. (*Journal of Tropical Medicine.*)

are scattered irregularly over limbs and trunk; occasionally they may be almost confluent, the patches coalescing and giving rise to an appearance as if the entire skin had been dusted over with flour. On the other hand, this furfuraceous desquamation may be so slight as to be overlooked. In other instances it may be very marked, the heaping up of desquamating epidermic scales producing white marks, very evident on the dark skin of a negro or Oriental.

This patchy, furfuraceous condition of the skin occurs not only at the early stages of yaws, but it

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may persist throughout the attack, or reappear as a fresh eruption at any period of the disease.

The yaw (Fig. 68).—When the furfuraceous patches have been in existence for a few days minute papules appear in them. Describing these papules, Nicholls remarks that, in examining them with a

Fig. 69.—Another case of Yaws.

lens, "they are seen to be apparently pushed up from the rete Malpighii through the horny epidermis, which breaks over their summits and splits in radiating lines from the centre, the necrosed segments curling away from the increasing papule. When the papules become about a millimetre in height and breadth, a yellow point may be observed on the summits . . . consisting not of a drop of pus under

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the epidermis . . . but of a naked, cheesy-looking substance, which cannot be wiped away unless undue force be used. Frequently a hair will be observed issuing from this yellow substance, thereby indicating that the hair follicles are the centres of the change going on." This papular eruption may persist during the entire attack, or it may appear at any time during the course of the disease. When extensive and occurring late, it indicates a protracted attack.

The papule, having arrived at this stage, may either cease to grow, the apex becoming depressed, cupped, and lined with the yellow cheesy material alluded to; or it may go on, increasing in size, to the formation of the typical yaw. In the latter case the lesion gradually grows into a rounded excrescence, the yellow material at the top widening out so as to form a complete cap encrusting the little tumour. The yaw so formed may be no larger than a split pea; or it may attain the breadth of a crown piece. The smaller tumours are hemispherical; the larger are more flattened or even depressed at the centre, possessing everted, somewhat overhanging, rounded edges. Occasionally, though rarely, a big yaw may include an area of sound skin. Several yaws may coalesce, and together cover a large and irregular surface, as an entire cheek, a popliteal space, or the dorsum of a foot. In the case of these large yaws, the surface of the growth is apt to be irregular and fissured. The neighbourhood of the mouth and anus are favourite sites for coalescent yaws; in such situations the moisture of the parts softens and removes the crust wholly or in part, so that the surface, in addition to being fissured, may be more or less bare, sodden, and fungoid.

The crust which caps and encloses an uninjured yaw is yellowish, granular, blotched with blood stains and encrusted dirt. At first the crust is somewhat moist, but gradually it becomes dry, brown, and even black. The crusts are firmly adherent, requiring some force to remove them; a proceeding which, though painless, may entail a little oozing of blood. Deprived of its crust the little swelling is seen to be

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red in colour, and generally smooth and rounded on the surface. According to size, it stands out anything from one-eighth to six-eighths of an inch above the surrounding healthy skin. Immediately after removal of the crust the exposed surface begins to pour out a pale, yellowish-grey, viscid fluid which soon becomes inspissated, rapidly forming a fresh cap to the yaw. Pus, unless as a consequence of irritation, is not, as a rule, found under the crust.

Although the formation of the papules and yaws is attended with much itching, the yaw itself is not at all sensitive; the tumour may be touched, with acid even, without causing pain—a diagnostic point of some importance.

The yaw usually attains its maximum development in two weeks. For several weeks longer it remains stationary before beginning to shrink. The crust then thins, shrinks, darkens, separates at the periphery, and at last falls off, disclosing at the site of the former fungating mass a slightly thickened spot of fairly sound skin which, though pale at first, may subsequently become hyperpigmented.

Ulceration.—Such is the normal process of evolution and involution of a yaw. But it sometimes happens that the tumours, in place of becoming absorbed, break down and ulcerate, the ulceration, however, being confined to the yaw itself. In other instances ulceration goes deeper and extends circumferentially, giving rise to extensive sores with subsequent cicatricial contractions. Such ulcerations may or may not be encrusted. With the development of the deeper and wider forms of ulceration, the typical lesions of yaws may disappear for a time, or perhaps permanently. In the latter case the ulcers are said not to be infective, and do not communicate yaws; they are, therefore, to be regarded rather as complications or, it may be, sequelæ. Such ulcers may persist for years. Ulceration, according to Nicholls, occurs in about 8 per cent. of cases.

Onychia.—Yaws may occur around or under a nail and give rise to a troublesome form of onychia.

Foot yaws.—When a yaw develops on the sole of

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a foot, in consequence of being bound down by the dense and thick epidermis it causes much suffering. Spreading laterally under the thick, leathery, and unyielding epidermis, it may attain a large size. After a time the epidermis over the growth gives way, splitting in a radiating fashion. Pressure being thus removed, the yaw fungates, and suffering diminishes.

A cracked scaly condition of the hands and feet, sometimes persisting for years, is not unusual in negroes, and must not be confounded with yaws, although not unfrequently the two conditions co-exist.*

Distribution.—The yaws may be scattered over the whole body; or the crop may be limited to one or two growths; or they may be confined to a circumscribed region of the skin. They are commonest on exposed parts, on the anterior surface of the body, and on parts especially liable to injury, as the feet and legs. They are most frequently found on the lower extremities; rarely on the scalp, and still more rarely in the axillæ. They are hardly ever seen on mucous surfaces unless about the lips, around the angles of the mouth, and in the nostrils, where they often form clusters.

Duration and recurrences.—Yaws lasts for weeks, months, or years, its duration depending on the general health, idiosyncrasy, hygienic conditions, and the treatment employed. Mild cases in healthy subjects finish in about six weeks. In other instances, especially in the debilitated, the disease runs on for months, successive crops of eruption being evolved. Sometimes these recurrences may stop short at the stage of desquamation, or at the papular stage, or they may proceed to the formation of typical yaws. The recurrences are usually preceded by feverishness,

* In the course of time the West Indian negroes have adopted a peculiar jargon—a mixture of French, English, and Spanish—to designate the various manifestations of yaws. The scaly patches are known in some of the islands as "pian dartres," in Jamaica as "yaws cacca"; the papular stage of eruption as "pian gratelle"; when the papular eruption occurs as a late symptom, it may be called "pian charaib," or "guinea-corn yaws." The developed yaw is sometimes known as "bouton pian." "Tubboes," "tubba," "crabs," "crappox," "crabes are

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pains in the bones and joints; and the successive crops may either be limited and partial in their distribution, or they may be general. In Fiji, Daniels states, the average duration of an attack of yaws is about one year.

The general health.—Except during the initial fever, or during one of the recurring febrile relapses, the general health is not as a rule affected. Occasionally, however, there is debility and cachexia; or there may be enlargement and tenderness of the lymphatic glands. In other instances the rheumatic pains are a principal feature, and may be very severe.

Persistent yaws.—That yaws sometimes effects a permanent hold is shown by the persistency with which it occasionally continues to recur during many years. In such cases the lesion has always the characters of a true yaw, and cannot be regarded as a "secondary" or "tertiary" manifestation in the sense in which these terms are applied to the late lesions of syphilis.

Powell describes two cases, mother and child, in whom, concurrently, a uniform swelling of the proximal phalanges of both hands occurred during the third year of an attack of yaws. To the touch the bones gave the impression of being rarefied. The swellings yielded to mercury.

Question of a primary sore.—An interesting point in the symptomatology of yaws is the question of the occurrence of a primary sore, as in syphilis. Numa Rat says there is such a sore, but that it is usually overlooked. He describes it as a papule with a pale yellow material at its apex, which may remain a papule, or which, after seven days, may ulcerate and

expressions applied to the painful manifestations on the soles of the feet. Forms of chronic dermatitis on hands and feet are called "dartres," "tubboe," "crabs," "dry tubboes," or where exudation goes on between cracks in soles or palms, "running crab yaws." A large persistent yaw is sometimes known as the "mother," or "grandmother," or "mama-pian"; smaller yaws as "daughter" or "granddaughter" yaws. Yaws which show themselves some time after the disease appears to have subsided are called "memba" (remember) yaws. Yaws coalescing in the form of a ring are called "ringworm" yaws.

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subsequently cicatrise. Other observers do not agree with this. They say that though yaws virus applied to a pre-existing ulcer may render it unhealthy-looking and cause it to fungate like an ordinary yaw, yet successful puncture inoculations, although they sometimes give rise to a yaw at the point of inoculation, do not by any means always produce a local lesion, much less an ulcer. Formerly it was thought that the lower animals were not susceptible to yaws. Several observers, including Castellani, have now shown that monkeys, even of a low order, can be successfully inoculated.

Question of sequelæ.—Mention is often made of nodes, of gummatous-like thickenings, and of punched out, serpiginous and lupoid ulcerations in connection with yaws. Most recent authorities regard all such phenomena as being generally the results of an independent, though concurrent, syphilitic or tubercular infection.

Destructive ulcerous rhino-pharyngitis (Leys).—This disease, which has been regarded by some as a sequel of yaws, generally commences as an ulcer on the soft palate. Slowly spreading it may make a clean sweep of the hard palate, of the soft parts, cartilages and bones of the nose, sparing the upper lip which is left as a bridge across a great chasm the floor of which is formed by the intact tongue. The disease may be arrested spontaneously at any period of its progress and long before so extensive a mutilation as that described has been effected; but it is always a long-standing and chronic affair and may linger as an indolent ulceration for years. As a rule, the larynx is spared; but, although phonation may be retained, articulation is seriously impaired.

This disease is very common in parts of the West Indies—Dominica for example (60 cases in a population of 2,000, Numa Rat), Guam, where it is known as *Gangosa* (1·5 per cent. of the population, Leys), the Carolines, Fiji, British Guiana and, undoubtedly, many other parts of the tropics. I believe I have seen the same condition in South China.

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It occurs at any age from childhood to 80. Leys saw it in Guam in children of three, four and nine years respectively.

The lesion has been attributed to leprosy, tuberculosis, syphilis and yaws. Against its being a leprous disease is the circumstance that it is not attended by any of the other phenomena of leprosy. Against its being of a tuberculous nature is the circumstance that it is confined to the tropics Against its being syphilis is the practical absence of syphilis among the natives of Fiji, where this form of ulceration is particularly common. Against its being a sequel of yaws is the want of correspondence in the proportional prevalence of the two diseases; for, although ulcerative rhino-pharyngitis is common in some places in which yaws is common, it is rare in other places where yaws is common, and common in other places where yaws is rare. For these and other reasons Leys has thrown out the suggestion that destructive rhino-pharyngitis of the tropics is an independent disease produced by a special micro-organism as yet undetected, and not, as has been supposed, a sequel of yaws.

Mortality.—Although in the literature of the subject reference is made to deaths from yaws, yet, judging from the statistics collected by Nicholls, the mortality must be very small indeed. In 7,157 West Indian cases, treated in various yaws hospitals, there were only 185 deaths—a mortality of 25·8 per thousand; a death-rate, as Nicholls points out, less than the average annual death-rate in one of the islands—Antigua. Doubtless although yaws itself seldom proves directly fatal, intercurrent diseases, such as sloughing phagedæna and phagedænic ulceration, predisposed to by the skin lesions, occasionally do so. If the verruga of Peru be a form of yaws, then, under certain conditions, yaws becomes a very dangerous disease.

Morbid anatomy and pathology.—No visceral changes have been found peculiar to yaws, although, of course, when yaws concurs with syphilis, gummata, etc., may be found; in this case the con-

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current gummata belong to the syphilitic and not to the yaws infection.

The tumours on the skin are granulomata made up of round or spindle-shaped cells, held together by a small amount of connective tissue and abundant blood-vessels. The focus of the circumscribed cell proliferation is the papilla, which becomes very much swollen, and the Malpighian layer.

Diagnosis.—A painless, insensitive, larger or smaller, circular, encrusted, red granulomatous excrescence occurring in the endemic district is almost certainly yaws. The most important point in connection with yaws, both as regards diagnosis and ætiology, is its relationship to syphilis. It has been, and is still held by some distinguished authorities, Hutchinson for example, that yaws is syphilis modified by race and climate. Certain features which the two diseases have in common are pointed to, and, doubtless, the recent discoveries of a spirochæta in association with both diseases will be adduced, in support of this contention. So far as clinical and microscopical evidence goes, it is decidedly in favour of, not to say conclusive for, regarding the two diseases as specifically distinct. There are many points of contrast in their clinical features. I may mention the primary sore, the infection of the fœtus, the adenitis, the exanthem, the alopecia, the absence of itching, the iritis, the affection of the permanent teeth, the bone and eye affections, the congenital lesions, the polymorphism of the eruptions, the nerve lesions and the gummata of syphilis. All these are wanting in yaws. Moreover, both diseases may concur in the same individual (Powell cites two cases, and Charlouis two, of syphilis supervening on yaws); and antecedent syphilis certainly does not confer immunity as against yaws, nor antecedent yaws against syphilis. Monkeys inoculated with yaws are not immunised against syphilis. Yaws may die out in a community, as in British Guiana (Daniels), yet syphilis remain; yaws may be universal in a community, as in Fiji, and yet true syphilis, whether as an acquired or congenital

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disease, be unknown. Finally, syphilis has never been shown to give rise to yaws, nor yaws to syphilis; neither, so far as known, has yaws been evolved in any community from syphilis, or appeared independently where the possibility of its having been introduced from a recognised yaws centre could be excluded with certainty.

The therapeutical argument for the identity of the two diseases is a very fallacious one. Sulphur will cure scabies and pityriasis versicolor; yet from this circumstance we may not conclude that these diseases are identical. The same may be said in respect of the influence of mercury and iodine on syphilis and on yaws.

Prophylaxis.—This resolves itself into the adoption of measures to prevent contagion. These are: the isolation and segregation of the affected; the dressing and treatment of wounds in the hitherto unaffected; the application of antiseptic ointments to yaws sores, so as to obviate the diffusion of germs; the purifying or destruction by fire of houses or huts notoriously infected; the prevention of pollution of bathing water by yaws discharges.

Treatment.—All are agreed as to the propriety of endeavouring by good food, tonics, and occasional aperients to improve the general health. Most are agreed as to the propriety of endeavouring to procure a copious eruption by stimulating the functions of the skin by warm demulcent drinks; by a daily warm bath with plenty of soap; and, during the outcoming of the eruption, by such diaphoretics as liquor ammoniæ acetatis, guaiacum, etc. Confection of sulphur is also recommended as a suitable aperient; it may be taken frequently in the early stages of the disease. All are agreed as to the propriety of avoiding everything—such as chill—tending to repress the eruption; warm clothing is therefore indicated. Many use mercury, or potassium iodide, or both, after the eruption is fully developed. These drugs have undoubtedly the power of causing the eruption in yaws to resolve. Some practitioners rarely use them, or, if they use them, do so only at the latest

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stages of the disease, considering that relapses are more prone to occur after their too early employment. Mercury, owing to its proneness to cause anæmia, is less frequently employed than potassium iodide. Where the eruption is persistently squamous, or papular, arsenic is frequently prescribed. Some touch the yaws with sulphate of copper; some apply nitrate of mercury ointment; others iodoform ointment; others leave them alone, confining their local measures to the enforcement of cleanliness. When the soles of the feet are attacked, the feet ought to be soaked in warm water to soften the epidermis, which should then be cut away sufficiently to liberate the subjacent yaw. Ulceration must be treated on ordinary principles. During convalescence, iron, arsenic and quinine are indicated.

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CHAPTER XXXVII

VERRUGA PERUANA

In certain narrow valleys of the Andes, between the ninth and sixteenth parallels of south latitude, and at an elevation of from 3,000 to 10,000 feet, an aggravated form of a disease in some respects closely resembling yaws, and locally known as "verruga," is endemic.

The **geographical distribution** of verruga, so far as known, is singularly limited; it is confined to certain valleys, the inhabitants of neighbouring places being exempt. It is said that the disease may be acquired in merely passing through the endemic districts; and that, unlike yaws, the domestic animals in these districts, as well as the human inhabitants, are subject to the disease.*

It has been suggested that the disease of which Carrion died was a septicæmia, that Oroya fever is typhoid to which yaws is superadded, that verruga is an expression of some form of helminthiasis, of trypanosomiasis, of spirillosis. Until the germ has been definitely recognised the exact nature of this disease cannot be determined.

Symptoms.—The peculiar initial rheumatic-like pains and fever are apparently the same in character as those of yaws, only more severe. Just as in yaws, one attack of verruga confers practical immunity. The constitutional symptoms likewise subside on the

* Two elaborate memoirs on this disease have appeared —"La Maladie de Carrion," and an article in *La Presse Médicale* (July 27th, 1898), both by Dr. M. E. Odriozola. It is curious that, although animals are said to be subject to the disease, Carrion chose to experiment on himself. No mention is made in the works referred to of experiments on animals, although Carrion is lauded for his enthusiastic devotion. The reader might consult an article in Pasteur's "Annales" (Sept. 25th, 1898), "Note sur la Bactériologie de Verruge du Pérou," by M. Charles Nicolle.

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appearance of the skin lesion, which, judging by the published descriptions, is a granuloma macroscopically and microscopically identical with that of yaws. Just as in the latter disease, the eruption may be sparse or abundant, discrete or confluent. As in yaws, individual granulomata may fail to erupt; others may subside rapidly; others, again, may continue to increase, and then, after remaining stationary for a time, gradually wither, shrink, and drop off without leaving a scar. If difference there be in their clinical features between verruga and yaws, apparently it is more one of degree than of kind.

In verruga the initial fever may continue for weeks, or even for months. It is very severe in many instances. Often it exhibits features like those of a malarial infection, including intermittency, profound anæmia, and sometimes enlargement of the spleen and liver. Very probably in such cases it is the outcome of a compound infection—verruga attacking a malarial subject. Not unfrequently in the endemic district a certain type of fever, believed to be verruga fever, proves fatal before the appearance of definite skin manifestations such as would justify a positive diagnosis. This was apparently the case with a medical student, named Carrion, who inoculated himself with blood from a verruga granuloma. The symptoms in his case closely resembled those of the very deadly fever referred to, which is known locally as Oroya fever.

In addition to the severity of the fever and rheumatic pains, the Peruvian disease is remarkable for the tendency to spontaneous hæmorrhage exhibited by the skin lesions. Apparently this peculiarity is attributable, like the hæmorrhages in the affection known as "mountain fever," to the diminished atmospheric pressure at great altitudes; for when the patients descend to the lower valleys, or to the sea level, the tendency to bleeding ceases. Possibly the unusual vascularity of the swellings, which are sometimes permeated by a network of cavernous sinuses, also arises from the same circumstance.

In yaws we find no mention made of the occur-

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rence of fungating granulomata in any situation but the skin. In verruga it would seem that the tumours may develop on mucous surfaces—in the œsophagus, the stomach, intestine, bladder, uterus, and vagina. Hence the dysphagia—a common symptom—and the occasional occurrence of hæmatemesis, melæna, hæmaturia, and bleeding from the vagina in the last-named disease.

Treatment.—It appears that cold tends to repress the development of the eruption, and that until this appears fever and pain persist. For this reason, as well as to avoid the hæmorrhage from the lesions when they do erupt, the patients should quit the heights and descend to near the sea level. External hæmorrhages, when they do occur, must be treated by graduated pressure; otherwise, the local as well as the general treatment is the same as for yaws.

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CHAPTER XXXVIII

ULCERATING GRANULOMA OF THE PUDENDA

Geographical distribution.—Drs. Neal, Ozzard, Conyers, and Daniels describe a peculiar form of ulcerating granuloma affecting more particularly the pudenda in dark-skinned races. Their observations were made in British Guiana, and principally on West Indian negroes. Daniels believes that he has seen a similar or the same disease in Fijians. The "serpiginous ulceration of the genitals" referred to by Macleod, and recently by other writers in India, more especially by Maitland, is the same, or a similar disease, examples of which I can recollect having seen in South China. Taylor, of New York, has seen it in whites in the United States, Goldsmith has met with it in aboriginals in North Australia, and Renner in West African negroes. Doubtless, therefore, although hitherto little notice has been taken of this disease, it is widely distributed in the tropics.

Ætiology.—There is reason for believing that the disease is generally, though not invariably, a venereal one. Maitland has seen it in the mouths of a husband and wife. He considers it may be inoculated on other forms of venereal sore, such as an ulcerating bubo, and that a compound sore may result. The nature of the virus has not been determined.

Spirochætes resembling *S. pallida* and *S. refringens* have been described by Wise as occurring in the ulcerations in British Guiana, but the nature of their relation to the disease has not been made out.

Age and Sex.—Ulcerating granuloma has not been observed before puberty; it has been found only after thirteen or fourteen, and up to forty or fifty. It occurs in both sexes, but particularly in women.

Symptoms.—The disease commences in the

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great majority of cases somewhere on the genitals, usually on the penis or labia minora, or on the groin, as an insignificant, circumscribed, nodular thickening and elevation of the skin. The affected area, which on the whole is elevated above the surrounding healthy skin, and is covered with a very delicate, pinkish, easily-rubbed-off epithelium, excoriates readily, exposing a surface prone to bleed and break down, although rarely ulcerating

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Fig. 70.—Ulcerating granuloma of the pudenda in the male.

deeply. The disease advances in two ways: by continuous eccentric peripheral extension, and by auto-infection of an opposing surface. In its extension it exhibits a predilection for warm and moist surfaces, particularly the folds between the scrotum and thighs, the labia, and the flexures of the thighs (Fig. 70). Its extension is very slow, years elapsing before it covers a large area. Concurrently with peripheral extension a dense, contracting, uneven, readily-breaking-down scar forms

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on the surface travelled over by the coarsely or finely nodulated elevated new growth which constitutes the peripheral part of the diseased area. Occasionally islands of active disease spring up in this scar tissue ; but it is at the margin of the implicated patch that the special features of the affection are best observed. In a case of some standing there is found a large area of white or irregularly pigmented, perhaps excoriated, unsound, contracting, folded and dense cicatrix surrounded by a narrow, serpiginous,

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Fig. 71.—Ulcerating granuloma of the pudenda in the female.

irregular border of nodulated, somewhat raised, red, glazed, delicately skinned or pinkish, superficially ulcerated or cracked new growth.

In the case of the female (Fig. 71) the disease may extend into the vagina, over the labia, and along the flexures of the thighs. In the male it may spread over the penis, involve the glans, scrotum, and upper part of the thighs. In either sex it may spread in the course of years to the pubes, over the perineum, and into the rectum, the recto-vaginal septum in the female ultimately breaking down. At times a profuse watery discharge exudes and even drips from the surface of the new growth, soiling the

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clothes, soddening the skin, and emitting a peculiarly offensive odour. In this condition the disease, slowly extending, continues for years, giving rise to inconvenience and perhaps seriously implicating the urethra, vagina, or anus, but not otherwise materially impairing the health. The lymphatic glands do not become affected. The disease continues entirely local.

Histology.—On microscopical examination the new growth at the margins of the sore is found to be made up of nodules, or masses of nodules, consisting of round cells having large and, usually, badly-staining nuclei. These cells are embedded in a delicate fibrous reticulum. The nodular masses are, for the most part, covered by epithelium, their under surfaces merging gradually into a thick, dense fibrous stroma in which small clusters of similar round cells are here and there embedded. The growths, though very vascular, contain no hæmorrhages; and there are no signs of suppuration or of caseation, no giant cells, and no tubercle bacilli. In vertical section of the small nodules the round cell mass will be found to be wedge-shaped, the base of the wedge being towards the skin; the deep-lying apex is usually pierced by a hair or two. The growth is found around sebaceous follicles, blood-vessels, lymphatics, and sudoriparous glands; but it is specially abundant, and most deeply situated, around the hair follicles.

Donovan has described certain parasitic elements of undetermined nature, which he has recently demonstrated in scrapings from the deeper parts of the Madras form of these sores. The parasite (Fig. 72) is like a gigantic short bacillus with rounded ends, measuring 2 μ by 1 μ. It occurs in large mononuclear cells and in great profusion. The parasites are sometimes scattered irregularly through the protoplasm of the affected cells; more often they are arranged in little round clusters of 8 or 10. On deep staining, something like an elongated nucleus can be made out. Donovan does not claim that in this body he has discovered the germ cause of ulcerating granuloma; but the position it occupies and its peculiar characters are highly suggestive.

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Diagnosis.—Malignant and syphilitic ulcerations of the groin are common enough; the disease under notice, however, differs widely from these — clinically, histologically, and therapeutically. It is characterised by extreme chronicity—ten or more years, by absence of cachexia or of any tendency to cause death, by non-implication of the lymphatic system, and by non-amenability to

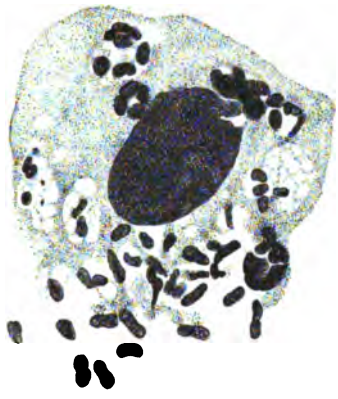

Fig. 72.—Parasitic elements in ulcerating granuloma of pudenda.

mercury and iodide of potassium. The disease which it most resembles is lupus vulgaris. From this it differs inasmuch as it is practically confined to the pudendal region; affects mucous as well as cutaneous surfaces; tends to follow in its extension the folds of the skin; is not associated with the tubercle bacillus, giant cells, caseation, or other evidences of tuberculous disease.

Treatment.—This disease is very rebellious to treatment. Scraping and caustics, including the actual cautery, have been freely employed; but, although some improvement may be effected by these means, new nodules almost invariably spring up in the resulting cicatrix. Until recently complete excision, where practicable, offered the best chance of permanent cure; of course, such a proceeding had to be under-

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taken before large areas and important passages had become involved. Conyers and Daniels found that camphor and carbolic acid in equal parts, and salicylic acid in unguentum creasoti, thirty to forty grains to the ounce, gave the best results; although in no instance have they succeeded in effecting a complete cure, the growth invariably recurring in the scars soon after discontinuance of treatment. Maitland recommends the repeated application of Vienna paste followed by boric acid poultices. Mercury and iodide of potassium are useless.

Judging from its relatively superficial nature and close resemblance to lupus, it seemed probable that ulcerating granuloma might prove amenable to some form of radiotherapy. This is actually the case, and X-rays are now regularly and successfully employed in Madras in the treatment of the disease. Of thirty-seven cases treated in this way in Madras Hospital in 1908 all proved successful within an average period of two months. In three of the cases which could be followed up there was no recurrence four months after their discharge.

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CHAPTER XXXIX

ORIENTAL SORE

Definition.—A specific ulcerating granuloma of the skin, endemic within certain limited areas in many warm countries. It is characterised by an initial papule, which, after scaling and crusting over, generally breaks down into a slowly extending and very indolent ulcer. Healing after many months, it leaves a depressed scar. The sore is inoculable and, usually, protective against recurrence.

Geographical and seasonal distribution.—Among the endemic places may be named Morocco, the Sahara (Biskra, Gafsa), Egypt, Crete, Cyprus, Asia Minor, Syria (Aleppo), Mesopotamia (Bagdad), Arabia, Persia, the Caucasus, Turkestan, India (Lahore, Multan, Delhi, etc.). Locally, Oriental sore is often called after some town or district in which it is specially prevalent; thus we have Delhi boil, Bagdad boil, and so forth. It is much more common in cities than in the country. In Bagdad few escape an attack; visitors, even of a few days only, are almost certain, at particular times of the year, to contract it. Juliano describes the disease as being common in Bahia, Brazil; the name Oriental sore, suggested by Tilbury Fox, is therefore no longer quite appropriate.

According to Hirsch, in the tropics this form of ulceration is specially prevalent about the commencement of the cool season; in more temperate climates, towards the end of summer or beginning of autumn. Years of prevalence may be succeeded by years of comparative rarity; possibly in harmony with altered sanitary conditions. In Delhi, for example, in 1864 from 40 to 70 per cent. of the resident Europeans were affected with the local sore; on certain sanitary improvements being effected, the

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frequency of the disease was immediately materially reduced.

Histology; ætiology.—Section of the papule displays an infiltration of the derma by a mass of small round granulation cells. These lie between the elements of the tissues, particularly about blood-vessels, lymphatics, and sweat glands; towards the centre of the lesion they completely replace the normal structures. Various micro-organisms have been described in association with Oriental sore. By staining sections in gentian violet and afterwards partly decolorising in spirit, Cunningham and Firth found certain violet-stained bodies (*Helcosoma tropicum*), varying in size and grouping, in a proportion of the infiltrating cells. These bodies Cunningham was inclined to regard as parasites. Riehl looked upon them as the result of a hyaline degeneration of protoplasm, and advanced a claim for certain micrococci which he said he found in great profusion in the granulation cells. That Cunningham's view is correct was proved by an American observer, H. Wright, who, in 1903, found in the granulation cells of an Oriental sore the Leishman body (Cunningham's parasites) in great profusion. This observation has been abundantly confirmed in India and elsewhere. Recently I have found these parasites in three cases of Oriental sore, one from near Delhi, one from Bushire, a third from Quetta. So that it may now be considered as definitely established that the cause of Oriental sore is the Leishman body, or a body morphologically identical with this parasite. James found it in 11 out of 18 ulcers examined; as it is possible that the 7 ulcers in this group of cases in which it was not found were not true Oriental sores, or that they were in process of healing, they cannot be brought forward as invalidating this conclusion. For the characters of the Leishman body *see* the chapter on Kala-azar, and the frontispiece.

In what way, under natural conditions, the parasite enters the tissues it is as yet impossible to state definitely. Not improbably it is conveyed by flies or other biting insects, and by them either inserted

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into the skin or applied to some pre-existing wound or sore. Dogs and camels are subject to this or a similar disease; it must not be overlooked that in them, or in other animals, may lie an important source of infection.

Probably there are two methods of infection, (*a*) *direct*, the Leishman body being directly inoculated without undergoing sexual or other developmental change; (*b*) *indirect*, in which a fly, bug or other insect, having ingested the parasite, conveys it, either itself or through its progeny, after the parasite has undergone evolutionary changes to the new host.

As a rule, second attacks do not occur. Observing this, the Jews of Bagdad at one time practised on their young children Oriental sore inoculation.

Neither race, nor sex, nor age, nor occupation, nor social condition materially influences susceptibility.

Incubation period and constitutional symptoms.—The incubation period of Oriental sore is variously stated in days, weeks or months. That it may be a brief one, a few days or weeks, seems to be established by the appearance of the sore within a short time of arrival in endemic districts, or after inoculation. That it can be of much longer duration is equally certain. I have seen an unquestionable Oriental sore which did not appear until five months after the patient had been exposed to any possibility of infection.

There is very little reliable information about the presence or absence of constitutional symptoms. It is customary to describe the disease as non-febrile. This may be true in most, but I am not convinced that it is so in every instance. It is obvious that in a disease with, at least in some instances, a very prolonged incubation period, slight, or even severe, fever might be overlooked or misinterpreted. Oriental sore produces an immunity against itself. There must therefore be profound constitutional change. In other diseases attended with similar change fever is almost invariably present at one time or another in their course. In the case just alluded to a severe anomalous fever, of five or six

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weeks' duration, preceded by eight months the appearance of the local lesions. Seeing, as has been pointed out (p. 187), the close connection of Oriental sore with kala-azar, this question of the constitutional symptoms in the milder disease is an important one, and should be carefully studied.

Symptoms.—The local lesion in Oriental sore commences as a minute, itching papule which tends to expand somewhat as a shotty, congested infiltration of the derma. After a few days or weeks the surface of the papule becomes covered with fine, papery scales. At first these scales are dry and white; later they are moister, thicker, browner, and adherent. In this way a crust is formed, which on falling off, or on being scratched off, uncovers a shallow ulcer. The sore now slowly extends, discharging a scanty ichorous material, which from time to time may become inspissated and crust over the sore, which continues to spread underneath. The ulcer extends by the erosion of its perpendicular, sharp-cut, and jagged edge, which is surrounded by a slight or more considerable areola of congestion. The surface of the ulcer is irregular. Any granulations which form speedily break down. Subsidiary sores may arise around the parent ulcer, into which they ultimately merge. These sores, usually about an inch or so in diameter, in process of time may come, in some instances, to occupy an area several inches across.

After a variable period, ranging from two or three to twelve or even more months, healing sets in. Granulation is slow and frequently interrupted. Often it commences at the centre whilst the ulcer may be still extending at the edge; often it is effected under a crust. Ultimately a depressed white or pinkish cicatrix is formed. Contraction of the scar, particularly if it happens to be on the face, may cause considerable and unsightly deformity.

Oriental sore may be single or multiple. Two or three are not uncommon; in rare instances as many as forty have been counted on the same patient. They are mostly situated on uncovered parts—hands,

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feet, arms, legs, and, especially in young children, on the face; rarely on the trunk; never on the palms, soles, or hairy scalp.

Dr. Sturrock, who practised in Bagdad for four years, informs me that in rare instances the disease recurs more than once, but, as a rule, the sores of the second attack do not break down. He has also seen a chronic type of the disease, which may recur and persist for several years and be associated with deposit in testes, in mucous membranes—such as the urethra and mouth—and, also, with a chronic form of dactylitis.

In a very few instances the initial papule does not proceed to ulceration, but persists as a scaling or scabbing, non-ulcerating, flattened plaque—just as sometimes happens in the case of the primary chancre of syphilis. Sometimes the ulcer is quite superficial, an erosion rather than an ulcer. Occasionally, from contamination with the virus of erysipelas, of sloughing phagedæna, or of some other infectious acute inflammatory skin disease, the primary lesion may become complicated and correspondingly modified, and perhaps a source of serious danger. Otherwise, Oriental sore is troublesome and unsightly rather than painful or dangerous.

Treatment.—Some have advocated destruction of the primary papule, and even of the ulcer, by caustics or by the actual cautery. It is doubtful if such a measure would prove effective. A knowledge of the nature and natural progress of the disease suggests a protective and soothing rather than an irritating line of treatment. A dressing with some mild antiseptic ointment, as of iodoform, boracic or salicylic acid, is indicated. Dr. Andrew Duncan informs me that in India he has seen these sores treated with great success by bandaging over them a piece of thin sheet lead. Most probably these sores were not true Oriental sores, which, as analogy would lead us to think, could heal only as the result of a specific treatment or on the establishment of immunity. Tonics when the patient is anæmic or debilitated, attention to the general health, change of climate should the disease persist beyond the usual time, are indicated.

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SECTION V.—ANIMAL PARASITES AND ASSOCIATED DISEASES

CHAPTER XL

1. PARASITES OF THE CIRCULATORY AND LYMPHATIC SYSTEMS

FILARIASIS

History.—Our knowledge of this subject dates from the discovery by Demarquay, in 1863, of a larval nematode—*microfilaria bancrofti* (Plate V.)—in the milky fluid from a case of chylous dropsy of the tunica vaginalis. Later, in 1866, Wücherer found the same organism in the urine of a number of cases of chyluria. In 1870 Lewis made a similar observation in India, and in 1872 discovered that the blood of man was the normal habitat of this larval parasite, which he named, accordingly, *Filaria sanguinis hominis*. Four years later Bancroft, in Brisbane (Queensland), discovered the adult form, and Cobbold named it *Filaria bancrofti*. Since that time the subject has rapidly expanded, and its great practical importance in tropical pathology is now recognised.

Nomenclature.—The writer has pointed out that Lewis's microfilaria* is not the only blood-worm in man, and that the human circulation is the habitat of the larvæ of no fewer than five, possibly of six or even more distinct species of filariæ. In consequence of this discovery, it was deemed advisable to modify the original name of Lewis's filaria. This

* The term *microfilaria* has been suggested by Le Dantec to designate the larval forms of the various nematodes whose young circulate in the blood. I adopt it as being a convenient expression.

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I proposed to call *Filaria nocturna* (Fig. 83); but as, in accordance with the rules of zoological nomenclature, precedence must be given to the name previously suggested by Cobbold for the adult form, I propose to call the larval form *microfilaria bancrofti* (Fig. 73, *a*). The other filariæ of the blood I named *F. diurna*

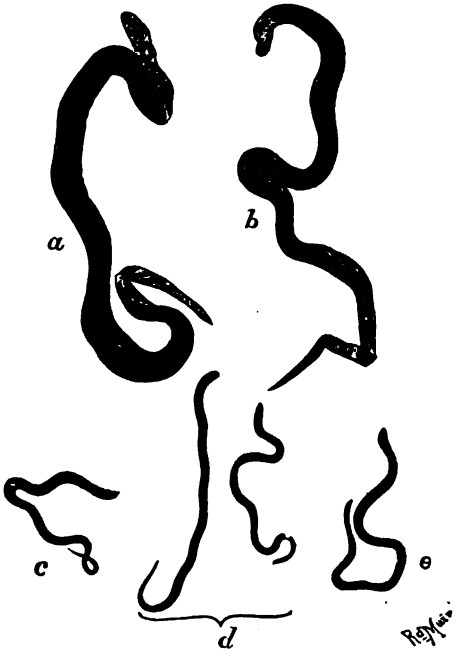

Fig. 73.—(*a*) Microfilaria bancrofti × 300; (*b*) microfilaria loa Africa × 300; (*c*) microfilaria demarquaii, St. Vincent × 300; (*d*) microfilaria ozzardi and microfilaria perstans, British Guiana × 300; (*e*) microfilaria perstans, Africa × 300.

(*mf. loa*), Fig. 73, *b*; *F. demarquaii* (*mf. demarquaii*), Fig. 73, *c*; *F. ozzardi* (*mf. ozzardi*), Fig. 73, *d* (a doubtful species); *F. perstans* (*mf. perstans*), Fig. 73, *e*; and *F. magalhaësi*, after its describer.

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Their pathological importance.—Only one of these parasites, so far as we know at present, appears to have important pathological bearings—*Filaria bancrofti*, which, in its adult stage, inhabits the lymphatics of man. As regards the others, with the exception of *F. loa*, we have no knowledge of any serious pathological significance they may possess. There can be no question of the importance in tropical pathology of *F. bancrofti*; there is abundant reason to believe that it is the cause of endemic chyluria, of various forms of lymphatic varix, and of other obscure tropical diseases, including, probably, elephantiasis.

FILARIA BANCROFTI (COBBOLD, 1877).

Synonyms—Filaria sanguinis hominis—F. nocturna—F. wiichereri.

Geographical distribution and prevalence.—The geographical distribution of *Filaria bancrofti* is very extensive. It has been found as an indigenous parasite in almost every country throughout the tropical and subtropical world, as far north as Spain in Europe and Charleston in the United States of America, and as far south as Brisbane in Australia. In many places—South China, for example—quite 10 per cent., and in other places half of the population harbour it. I have ascertained that it is probable that one-third of the inhabitants of at least one district in India—Cochin—carry blood filariæ. I also find that in some of the South Sea islands—Samoa, for example—fully one-half of the people are affected in this way. Thorpe has shown that in the Friendly Islands 32 per cent. of the people harbour this filaria. We have similar testimony as to the great frequency of the parasite in Madras from Maitland and others, in Demerara from Daniels, in several of the West India Islands from Low, in West Africa from Annett, Dutton, and Prout. Doubtless, if diligently and systematically sought for, it could be found in most tropical countries.

Demonstration of blood microfilariæ.

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PLATE V.—MICROFILARIÆ OF THE BLOOD.

1, mf. bancrofti; 2, mf. perstans; 3, mf. loa; 4, mf. demarquail.

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—Whoever would investigate the subject of filariasis will find that, in order practically to comprehend the subject and to provide himself with abundant material for observation, it is advisable to make systematic examination of the blood of the inhabitants of some district in which filariasis is endemic. If this be done, the observer is sure to come across, sooner or later, cases in which *microfilaria bancrofti* abounds, and also of the diseases to which it gives rise.

Technique.—I recommend the following procedure as likely to supply the investigator not only with material, but also with much useful information. Let him visit, *late in the evening*, some hospital, or prison, or other establishment where he can have an opportunity of examining the inmates, and let him procure slides of the blood of, say, 100 persons. The slides are conveniently prepared by pricking the finger of each person in turn, transferring large drops of the blood so obtained to ordinary microscope slips by simply dabbing the centre of the slip on the blood. The blood is then spread out with a needle so as to cover in a moderately thin film about a square inch of one surface of each slip. Each slip, so soon as the blood is spread, should be laid on its uncharged surface on a smooth, level surface until dry; it is then labelled and put aside. One preparation of this description may be made from each person, who should be selected simply as a representative of the general population, and therefore irrespective of his being physically sound, or of his being the subject of any particular type of disease.

The slides may be examined in various ways, either at once or, if more convenient, weeks or months afterwards; if kept dry and away from cockroaches, etc., they do not spoil. A convenient plan is to dip the slides, without previous fixing, in a weak solution of fuchsin—about three or four drops or more of the saturated alcoholic solution to the ounce of water. They are left in the stain for about an hour, and then examined wet and without cover-glass. If the slides are old, they may stain too deeply; in this case they may be partially decolorised in weak acetic acid—two or three drops to the ounce of water—and afterwards washed. Recent slides, if placed in water for a few minutes until the hæmoglobin is discharged, show the microfilariæ very well; it is advisable, however, for the novice at this sort of work to use, in the first instance, the fuchsin method described above.

Another plan is to fix the blood-film with alcohol, and then to stain by running on a few drops of saturated watery solution of methylene blue, washing off the superfluous stain after half a minute, and, if necessary, decolorising with weak acetic acid and washing; the wet slide is then examined with the microscope. Or, without previous fixing with alcohol, the slide,

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after it has dried, may be dipped for a few seconds in distilled water so as to wash out the hæmoglobin, dried, and then, with or without fixing, stained with methylene blue, logwood, or other suitable stain.

An inch or half-inch objective and a mechanical stage with a parallel movement will enable the investigator to pass rapidly in review the whole of the blood on the slide. In unfixed slides, if microfilariæ are present, they will be detected readily; the hæmoglobin of the blood corpuscles being dissolved out by the watery stain, the white blood corpuscles and any microfilariæ that may be present are the only coloured objects visible on the slide, and therefore at once catch the eye.

In any district in which the filaria is moderately common, out of 100 slides prepared in this way from as many individuals, probably eight or ten will be found to contain the parasite. When microfilariæ have been detected, the persons from whom the parasite-bearing slides came may be used afterwards as a source of supply for further examinations and study.

Demonstration of living microfilariæ.—When it is desired to study the living microfilaria, all that is necessary is to make three or four ordinary wet preparations of the blood of a filaria-infected person—making them during the evening or night, and ringing the cover-glasses with vaseline so as to prevent the slides from becoming dry. In such preparations the microfilariæ keep alive for a week, or even longer, and can readily be detected by their movements, an inch or half-inch objective being used in the first instance as a searcher.

Permanent preparations.—Permanent preparations may be made by fixing very thin films of blood with alcohol or heat, staining with methylene blue, eosin, etc., and mounting in xylol balsam. It is generally advisable before fixing to wash out the hæmoglobin with water or very weak acetic acid. Logwood is perhaps the best stain; it brings out the sheath very distinctly, and picks out the nuclei. Double staining with eosin and logwood shows very well the structure of the musculo-cutaneous layer of the worm, in addition to other anatomical details.

Description of larval form.—Examined in fresh blood, *microfilaria bancrofti* (Fig. 74) is seen to be a minute, transparent, colourless, snake-like organism, which, without materially changing its position on the slide, wriggles about in a state of great activity, constantly agitating and displacing the corpuscles in its neighbourhood. At first the movements are so active that the anatomical features of the microfilaria cannot be made out. In the course of a few hours the movement slows down, and then one can see that the little worm is shaped like a snake or an eel; that is to say, that it is a long, slender, cylindrical organism, having one extremity abruptly rounded off, and the other for about one-fifth of the entire length gradually tapered to a fine point. On measurement, it is found to be a little over or under 0·3 mm. in length

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by 0·008—0·011 mm. in diameter—about the diameter of a red blood corpuscle.

When examined with a low power, it appears to be structureless; with a high power a certain amount of structure can, on close scrutiny, be made out. In the first place, it can be seen that the entire animal is enclosed in an exceedingly delicate,

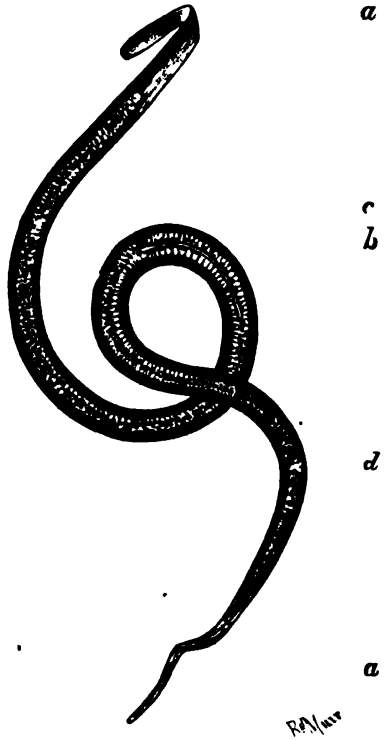

Fig. 74.—Anatomy of mf. nocturna.
a a, Sheath; *b*, central viscus; *c*, V spot; *d*, tail spot.

limp, structureless sack, in which it moves backwards and forwards (Fig. 74, *a*). This sack, or "sheath," as it is generally called, although closely applied to the body, is considerably longer than the worm it encloses; so that that part of the sack which for the time being is not occupied is collapsed and trails after the head, or tail, or both, as the case may be. It can be

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seen also that, about the posterior part of the middle third of the parasite, there is what appears to be an irregular aggregation of granular material which, by suitable staining, can be shown to be a viscus of some sort (Fig. 74, *b*). This organ runs for some distance along the axis of the worm. Further, if a high power be used, a closely set, very delicate transverse striation can be detected in the musculo-cutaneous layer throughout the entire length of the animal. Besides this, if carefully looked for at a point about one-fifth of the entire length of the organism backwards from the head end, a shining, triangular V-shaped patch (Fig. 74, *c*) is always visible. What may be this V spot is brought out by very light staining with dilute logwood. The dye brings out yet another spot (Fig. 74, *d*), similar to the preceding, though very much smaller; this second spot is situated a short distance from the end of the tail. The former I have designated the "V spot," the latter the "tail spot." These spots are probably connected with development, the V spot being the rudiment of the future water-vascular system, the tail spot that of the anus or cloaca and posterior part of the alimentary canal. The spots (Fig. 74, *c*, *d*) are not stained by strong logwood or by the anilin dyes. Staining with logwood also shows that the body of the little animal is principally composed of a column of closely packed, exceedingly minute cells enclosed in a transversely striated musculo-cutaneous cylinder (Fig. 74); at all events, many nuclei are thereby rendered visible. Low has recently pointed out to me that the break seen in all stained specimens in the central column of nuclei occurs at a point slightly anterior to the V spot. This break can only be recognised in stained preparations.

When the movements of the living microfilariæ have almost ceased, by careful focussing it can be seen that the head end is constantly being covered and uncovered by a six-lipped—or hooked—and very delicate prepuce; and, moreover, one can sometimes see a short fang of extreme tenuity, based apparently on a highly retractile granule, suddenly shot out from the uncovered extreme cephalic end, and as suddenly retracted (Fig. 74A, *c*, *d*).

Filarial periodicity.—A singular feature in the life of the microfilaria is what is known as "filarial periodicity."

If under normal conditions of health and habit the blood be examined during the day, the parasite is rarely seen, or, if it be seen, only one or two specimens at most are encountered in a slide. It will be found, however, that as evening approaches, commencing about 5 or 6 o'clock, the microfilariæ begin to enter the peripheral circulation in gradually increasing num-

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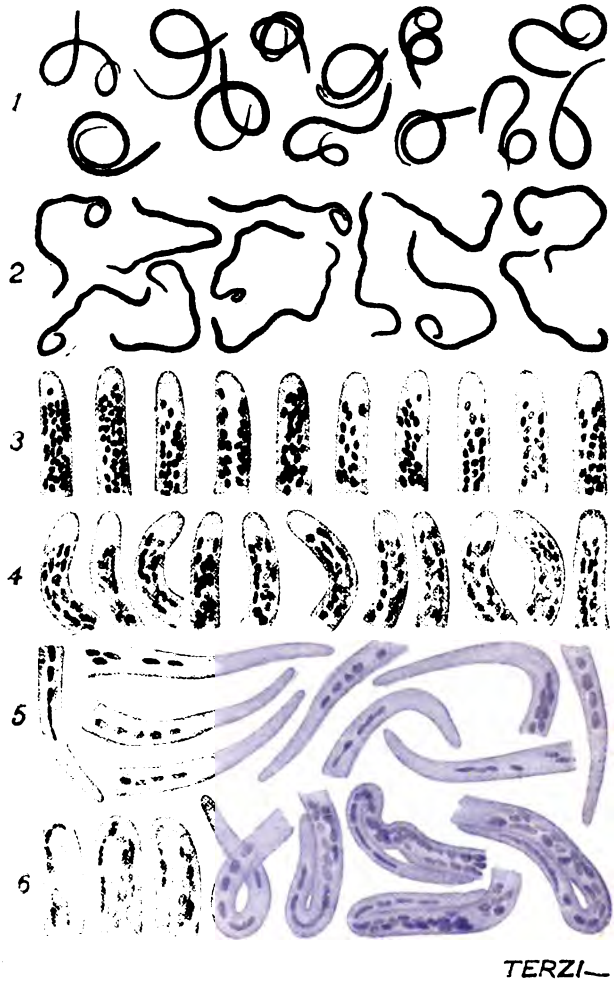

PLATE VI.—Distinguishing Features between mf. bancrofti and mf. loa, in Stained Specimens.

Attitudes (1) of mf. bancrofti, (2) of mf. loa; heads (3) of mf. bancrofti, (4) of mf. loa; tails (5) of mf. bancrofti, (6) of mf. loa.

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bers. The swarm goes on increasing until about midnight, at which time it is no unusual thing to find as many as three hundred, or even six hundred, in every drop of blood; so that, assuming that the parasites are evenly distributed throughout the circulation, it may be inferred that as many as forty or fifty millions are simultaneously circulating in the blood-vessels. After midnight the numbers begin gradually to decrease; by 8 or 9 o'clock in the morning the microfilariæ have disappeared from the peripheral blood for the day. This diurnal periodicity is, under normal conditions, maintained with the utmost regularity for years. Should, however, as Mackenzie

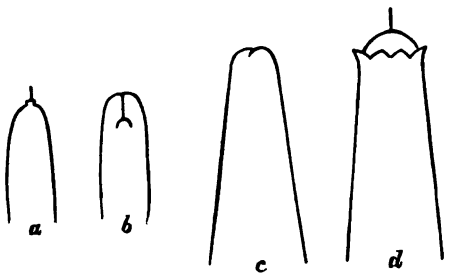

Fig. 74A.—Structure of head end of mf. perstans (*a*, *b*), and of mf. bancrofti (*c*, *d*).

has shown, a filarial subject be made to sleep during the day and remain awake at night, the periodicity is reversed; that is to say, the parasites come into the blood during the day and disappear from it during the night. It cannot be the sleeping state, as some have conjectured, that brings about this periodicity; for the ingress of the microfilariæ into the peripheral blood commences three or four hours before the usual time for sleep, and the egress several hours before sleep is concluded, and this egress is not complete until several hours after the usual time of waking. This night swarming of the larvæ of *F. bancrofti* in the peripheral circulation is an adaptation correlated to the life-habits of its liberating agent, the mosquito.

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Some years ago I had an opportunity of ascertaining that during their diurnal temporary absence from the peripheral circulation the microfilariæ retire principally to the larger arteries and to the lungs (Fig. 75), where, during the day, they may be found in enormous numbers.

The patient on whom this observation was made was the subject of lymph scrotum and varicose groin glands. His blood contained large numbers of embryo filariæ which exhibited the anatomical features and periodicity characteristic of *microfilaria bancrofti*. One morning he committed suicide by swallowing a large quantity of dilute hydrocyanic acid. Death was almost instantaneous. At the *post-mortem* examination, made six hours later, a huge lymphatic varix was found occupying the pelvis and back part of the abdominal cavity. In the dilated lymphatic vessels many adult filariæ—*F. bancrofti*—were found. The distribution of the microfilariæ was studied by counting them in drops of blood expressed from the various organs, and also in sections. The result is summarised in the following tables:—

ENUMERATION OF MICROFILARIÆ IN A DROP OF BLOOD EXPRESSED FROM THE FOLLOWING ORGANS.

Organ.	No. of Slides.	Aggregate no. of microfilariæ.	Average per Slide.
Liver	3	2	⅔
Spleen	3	3	1
Brachial venæ comites ...	4	111	28
Bone marrow	1	0	0
Muscle of heart	3	365	122
Carotid artery	1	612	612
Lung	10	6751	675

ENUMERATION OF MICROFILARIÆ IN SECTIONS OF THE FOLLOWING ORGANS.

Organ.	No. of Section.	Aggregate no. of microfilariæ.	Average per Section.
Liver	10	8	0·3
Spleen	4	0	0·0
Kidney	8	13	1·6
Brain	4	4	1·0
Muscle (voluntary)	3	2	0·33
Heart muscle	4	68	17 0
Lung	6	301	50·16
Lobe of ear	4	1	0·25
Scrotum	4	0	0·0

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In the lung sections (Fig. 75) the microfilariæ lay outstretched or variously coiled in the vessels, large and small. In the heart muscle they lay along the capillaries between the fibres; in the kidneys they seemed specially to affect the Malpighian tufts; a very few were found in the capillaries of the brain; vast numbers were found in smears from the inner surface of the carotid arteries. The preparations afforded no explanation as to how the microfilariæ contrive to maintain their position in the blood current, or as to the forces determining their peculiar distribution. Their absence from the liver and spleen is a remarkable fact.

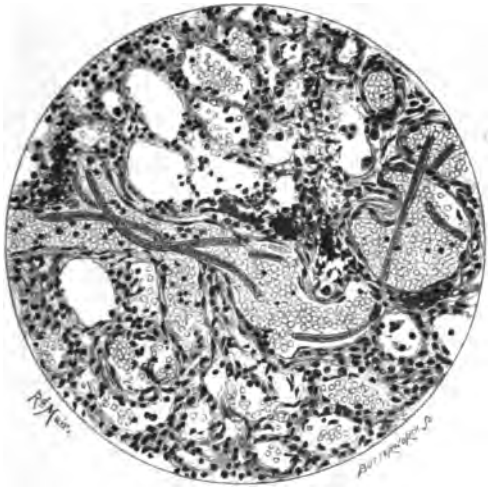

Fig. 75.—Section of lung showing microfilariæ in the blood-vessels. (*From a microphotograph by Mr. Spitta.*)

The mosquito the intermediary host of *Filaria bancrofti*.—Should the females of certain species of mosquito * which had fed on the blood of a filaria-infested individual be examined immediately after feeding, the blood contained in the stomach of the insects will be found to harbour large numbers of living filariæ. If one of these mosquitoes be examined three or four hours after it has similarly

* Several species of mosquitoes may subserve *F. bancrofti*. *Culex fatigans* is the first in which it was found.

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fed, it will be found that the blood corpuscles have in great measure parted with their hæmoglobin, and that the blood plasma in consequence of this and of dehydration has become thickened, though not coagulated. If attention be directed to the microfilariæ in the thickened blood, it will be seen that many of them are actively engaged in endeavouring to escape from their sheaths. The diffused hæmoglobin has so thickened the blood plasma that it has become viscid, and holds, as it were, the sheath. This change in the viscosity of the blood seems to prompt the microfilariæ to endeavour to escape from their sheaths. They become restless, as if excited. Alternately retiring towards the tail end and then rushing forward to the head end of the sheath, the imprisoned parasite butts violently against the latter in frantic effort to escape. After a time, the majority succeed in effecting a breach and in wriggling themselves free from the sheaths which had hitherto enclosed them (Fig. 76).* The microfilaria now swims free in the blood, the character

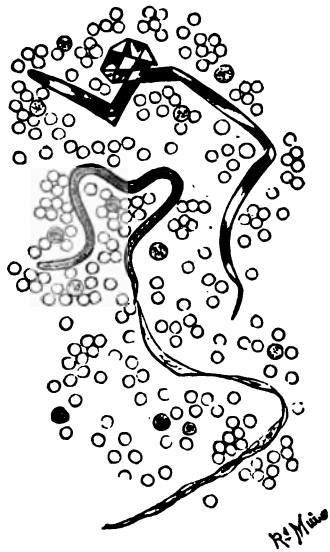

Fig. 76.—Filarial ecdysis.

* This casting of its sheath by the microfilaria can be induced in ordinary blood slides by chilling them on ice, or by otherwise bringing about the diffusion of the hæmoglobin. The following method is usually successful: Ring with vaseline the cover-glasses of several ordinary wet preparations of finger blood obtained at night from a filarial patient; wrap the preparations separately in filter paper and lay them, enclosed in a watertight tin box, on a block of ice for six or eight hours—say over night.

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of its movements once more undergoing a remarkable change. Hitherto, though active enough in wriggling about, the parasite did not change materially its position on the slide; but now, having become free, it moves about from place to place—locomotes, in fact. If we dissect a mosquito at a somewhat later period after feeding, it will be found that the stomach of the insect, though still full of blood, contains very few

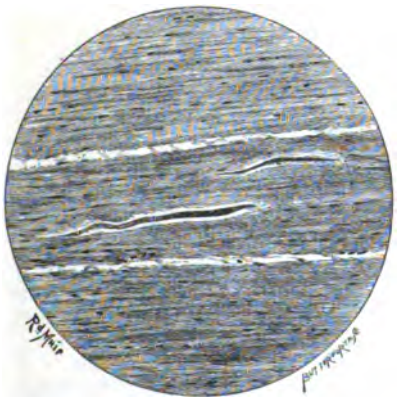

Fig. 77.—Section of thoracic muscles of mosquito, showing microfilariæ between the fibres: first day after the insect has fed on a filariated patient. (*From a microphotograph by Mr. Spitta.*)

microfilariæ, although their empty sheaths can be seen in abundance. If, however, we break up with needles the thorax of the insect and tease out in normal salt solution the muscular tissue, we shall find that the microfilariæ, after discarding their sheaths, have quitted the stomach and entered the thoracic muscles of the insect, among the fibres of which they are now moving languidly

Next morning examine them with the microscope. It will be found, as the chilled slides warm up, that wherever on the slides the hæmoglobin has become diffused and the blood lakey, the microfilariæ, as they gradually revive from the chilling, begin to endeavour to break through their sheaths. By evening most of them have effected this, and their empty sheaths can be seen lying scattered about in the viscid blood. The blood must not be frozen.

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(Figs. 77, 78, 79). By a course of serial dissections of filariated mosquitoes we can ascertain that in the thorax of the insect the parasite enters on a metamorphosis which takes from sixteen to twenty days (longer or shorter, according to atmospheric temperature) to complete—a metamorphosis eventuating in the formation of a mouth, of an alimentary canal, and of a peculiar trilobed tail, as well as in an

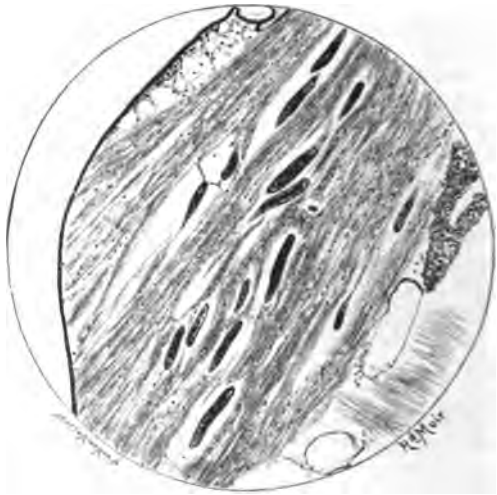

Fig. 78.—Section of thoracic muscles of mosquito seven days after it had fed on a filariated patient. (*From a microphotograph by Mr. Spitta.*)

enormous increase in the size (to $\frac{1}{16}$ of an inch) and activity of the young parasite. The filariæ now quit the thorax.

A few find their way to the abdomen, where, in properly prepared sections, they may occasionally be seen in the tissues around the stomach, and even among the eggs at the posterior part of the abdomen. The vast majority pass forwards by the prothorax and neck, and, entering the head, coil themselves up close to the base of the proboscis and beneath the pharynx and under-surface of the cephalic ganglia. Low, in sections prepared at the London School of

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Tropical Medicine from filariated mosquitoes sent to me by Bancroft, of Australia, has shown that the filaria in its future progress finds its way into the proboscis; an observation which has been confirmed by James in India and Annett and Dutton in West Africa. As pointed out by Grassi, its exact position here is the interior of the labium (Fig. 81, *a*). Apparently the filariæ seek to emerge (for such must be their object in entering the proboscis) in pairs; at all

Fig. 79.—Section of thoracic muscles of mosquito about twelve days after it had fed on a filariated patient. (*From a microphotograph by Mr. Spitta.*)

events, in those sections which I have examined, two worms were in each instance found together, their heads abreast of each other and close to the termination of the labium in the labella.

The parasites remain in this position awaiting an opportunity to enter a warm-blooded vertebrate host when the mosquito next feeds on such. This they appear to do by penetrating the thin membrane that unites the labella to the tip of the proboscis

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and so passing into the puncture made in the skin by the stilets.* Apparently the filariæ can discriminate between flesh and vegetable, for in mosquitoes fed on bananas the parasites had not been deceived into passing into so inhospitable a medium: up to forty days after the insect was infected, and after

Fig. 80.—Section of mosquito about sixteen days after it had fed on a filariated patient. The filaria has escaped from the thoracic muscles. (*From a microphotograph by Mr. Spitta.*)

many meals of banana, they could still be found coiled up in the head or stretched out in the labium.

These observations prove that, like the malaria

* Annett and Dutton pointed out that there is a weak point in the chitinous skeleton of the labium just where the labella are jointed on, and suggested that it is at this weak point that the parasites escape. Bancroft confirmed this suggestion by showing that the filariæ enclosed within the labium will escape readily at this point under the least pressure. Noè also, in a more recent paper, agrees with Annett and Dutton and rejects his former hypothesis (held in common with Grassi) to the effect that the filariæ escape through a rupture in the contiguity of the labium when it is buckled up during haustellation. Noè satisfied himself by numerous experiments that the filariæ invariably die when extruded at the seat of the bend. Finally, Lebredo, by actual experiment, proved that the filariæ escape in this way. He placed

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parasite, the filaria is introduced into its human definitive host by mosquito bite. Whether it

Fig. 81.—F. bancrofti in head and proboscis of mosquito.

a, *a*, *a*, filaria; *b*, labium; *c*, labrum; *d*, base of hypopharynx; *e*, duct of veneno-salivary gland; *f*, *f*, cephalic ganglia; *g*, *g*, eye; *h*, œsophagus; *j*, pharyngeal muscle.

may obtain an entrance by any other channel or medium it would be hard to prove and rash to deny. That the young filaria can live in water for a time is

living mosquitoes on slides, irrigated them with a weak saline solution and placed them on the stage of the microscope. He separated the various parts of the proboscis by a slight pressure so as to observe more clearly, and placed the flame of a Bunsen burner close to the slide. He noticed that the filariæ moved violently within the labium when the liquid in which the mosquito was bathed attained a higher temperature. Finally, one managed to pierce its way through at the tip of the labium and was soon followed by others. He noticed the escape of five filariæ within a minute. Sometimes two passed simultaneously. Too high a temperature killed both larvæ and mosquito. A fall of temperature arrested the process.

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certain; it is conceivable that some of them, s those which at the completion of their st development in the mosquito find their way in abdomen of the insect, may escape into water the mosquito lays her eggs or dies.*

Technique.—Mr. Max Colquhoun made for me beautiful illustrating the metamorphosis of the filaria in mosquit following technique. The insects, preserved in glycerii soaked in dilute acetic acid 5 per cent. for one day only; formalin 50 per cent., water 50 per cent., for one day; ne solute alcohol for one day; *absolute* alcohol and ether, equ one day; finally in celloidin for one day. They were then s placed in strong hæmatoxylin for two hours, decolourise hydrochloric (1 per cent.) and alcohol, washed in water through anilin oil, xylol, and mounted in xylol balsam. sections are not a success.

In working with fresh mosquitoes, all that is necessary is to up the thorax of the insect with needles in normal salt soluta and, after removing the coarse fragments of the integuments of th mosquito, apply a cover-glass and place under an inch objective The filariæ are readily detected. If the slide is dried, fixed, anc stained with a watery solution of some anilin dye or with log-wood, and mounted in xylol balsam, beautiful permanent preparations will be obtained.

Once introduced into the human body, the filaria finds its way into the lymphatics. Arrived in one of these, it attains sexual maturity, fecundation is effected, and in due course new generations of

* In my original observations on this subject in 1879 and 1883 (*Trans. Linnean Soc.*, 1883) I supposed that filarial metamorphosis, so far as the mosquito was concerned, is completed in from six to seven days. This I now believe was too short an estimate. Bancroft (*Journ. of Trop. Med.*, 1899) has since shown that it is necessary to feed the experimental mosquito (at all events, *C. fatigans*), so as to keep it alive for at least sixteen days, to obtain the final stages of the metamorphosis. I have little doubt now that the insects on which my observations were made had fed repeatedly, without my being aware of it, after their meal on the filariated patient. Bancroft has shown that by proper feeding (he used banana for the purpose) mosquitoes may be kept alive for several months, any filariæ they happen to harbour remaining alive, but not advancing in development beyond the final stage alluded to in the above description. In the observations referred to I conjectured that the fully metamorphosed filaria escaped from the insect either at her death or when she deposited her eggs, and that thus, in drinking-water, it obtained a chance of gaining access to the stomach of a human host. Before Low's observation Bancroft had very nearly guessed the truth, for he had expressed the idea that the filaria may be injected into man by the mosquito when it refeeds, or that it may be swallowed by man while it is still enclosed in its intermediary insect host.

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poured into the lymph. These,
glands—if such should intervene—
racic duct and left subclavian vein,
ics of the upper part of the body,
the circulation.

e history of *Filaria bancrofti*; man
, the mosquito its intermediary host.
filarial periodicity is an adaptation
e parasite to the nocturnal habits of
is also manifest that the purpose
ith which it is provided while cir-
man host is to muzzle the young

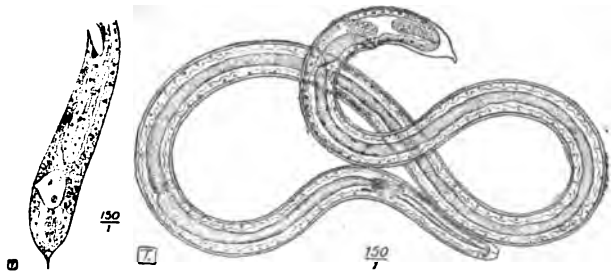

Fig. 82.—Stages of larval form of F. bancrofti, from the thoracic muscles of Culex fatigans (after Looss).

filaria and prevent its breaking through the blood-vessels, and thereby missing its chance of gaining access to the mosquito. The cephalic armature is adapted for piercing the walls of the mosquito's stomach, and for enabling the parasite to travel through the tissues of the insect.

Anyone desirous of working out for himself the metamorphosis of the filaria in the mosquito can readily do so, even in the absence of a suitable human subject, by setting Anopheles mosquitoes to bite filariated dogs. In most tropical countries a large proportion of the dogs harbour *Filaria immitis*, whose larvæ circulate in the blood and are taken up by mosquitoes in the same way as *F. bancrofti*. Grassi and Noè (confirmed by Bancroft, Sambon, and Low) have shown that the embryo *F. immitis* passes through the earlier stages of its metamorphosis in the Malpighian tubes of Anopheles, whence, on attaining a certain stage of development, it passes forward to the head of the insect, where it behaves in much the same way as *F. bancrofti*.

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Parental forms.—The parent filariæ have been found many times. They are long, hair-like, transparent nematodes, three or four inches in length (Fig. 83). The sexes live together, often inextricably coiled about each other. Sometimes they are enclosed, coiled up several in a bunch and tightly packed, in little cyst-like dilatations of the distal lymphatics (Maitland); sometimes they lie more loosely in lymphatic varices; sometimes they inhabit the larger lymphatic trunks between the glands, the glands themselves and, probably not unfrequently, the thoracic duct.

The *female filaria* is the larger, both as regards length and thickness. It measures 85-90 mm. in length by 0·24—0·28 mm. in breadth. The two uterine tubes, occupying the greater extent of her body, are filled with ova at various stages of development. In both sexes the oral end (Fig. 84, *b*) is slightly tapered, club-shaped and simple; the tail (Fig. 84, *a*, *c*) also is tapered to comparatively small dimensions, its tip being rounded off abruptly. The vagina opens on the ventral surface about 1·2—1·3 mm. from the anterior extremity; the anus just in advance of the tip of the tail. The cuticle is smooth and without markings.

Fig. 83.—F. bancrofti (natural size), *a*, male; *b*, female.

To the naked eye the *male worm* is characterised by its slender dimensions (about 40 mm. in length by 0·1 mm. in diameter), by its marked disposition to curl, and by the peculiar vine-tendril-like tail, the extreme end of which is sharply incurvated (Fig. 83, *a*).* The cloaca gives exit to two slender, unequal spicules (0·2 and 0·6 mm. respectively). The existence of caudal papillæ in the male worm has not as yet been satisfactorily ascertained. Looss describes three pairs of small conical postanal papillæ, but is uncertain whether there are any similar papillæ in front of the ano-genital orifice.†

Morbid anatomy and pathology.—*The filaria not generally pathogenic.*—In most cases of filarial infection the parasite exercises no manifest injurious influence whatever. In a certain proportion of instances, however, there can be no doubt that it

* According to Maitland, this incurvation of the tip of the tail is a *post-mortem* phenomenon.

† Looss is inclined to believe, from discrepancies in the descriptions of different authors from different parts of the world, that under the name *F. bancrofti* two or more species are being confounded.

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does have a very prejudicial effect on its host; and this mainly by obstructing lymphatics. The healthy, fully-formed microfilariæ—that is to say, the larval filariæ which, by means of the microscope, we see in the blood—have, so far as we can tell, no pathogenic properties whatever; the parent worm and the immature products of conception, alone, are dangerous.

Filarial disease originates in injury of lymphatic trunks.—Roughly speaking, the filaria causes two types of disease: one characterised by varicosity of lymphatics, the other by more or less solid œdema. The exact way in which the parasite operates has not been definitely and absolutely ascertained for all types of

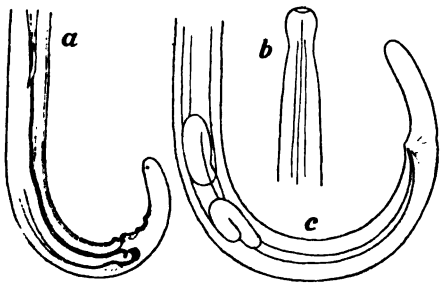

Fig. 84.—Parental forms of *F. bancrofti* (magnified).
a, Tail of male; *b*, head and neck; *c*, tail of female.

filarial disease. Apparently, in some instances, a single worm, or a bunch of worms, may plug the thoracic duct, and act as an embolus or originate a thrombus; or the worm may give rise to inflammatory thickening of the walls of this vessel, and so lead to obstruction from the consequent stenosis or thrombosis. In other instances the minor lymphatic trunks may be similarly occluded. As an effect of either form of occlusion, the lymphatic areas drained by the implicated vessels are cut off from the general circulation, and varicosity or œdema, or both ensue.

Pathology of lymphatic varix.—In consequence of the rich anastomosis existing between the

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contiguous lymphatic areas, on filarial obstruction occurring in one of them a compensatory lymphatic circulation is sooner or later established. But before this can be properly effected a rise of lymph pressure and a dilatation of the lymphatics in the implicated area must take place. This leads to lymphatic varix of different kinds, degrees, and situations. When the seat of filarial obstruction is the thoracic duct, the chyle poured into that vessel

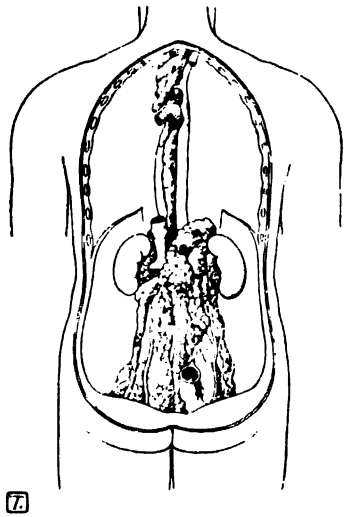

Fig. 85.—Dissection of the lymphatics in a case of chyluria, showing the dilated right and left renal lymphatics and thoracic duct. (*Mackenzie, Trans. Path. Soc., Lond.*)

can reach the circulation only by a retrograde movement; consequently, this fluid may be forced to traverse in a retrograde way the abdominal and pelvic lymphatics, the lymphatics of the groin, scrotum, and abdominal wall. As a consequence, these vessels, together with the thoracic duct up to the seat of obstruction, become enormously dilated. In dissections of such cases (Fig. 85) the thoracic duct has been found distended to the size of a finger, the

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abdominal and pelvic lymphatics forming an enormous varix, perhaps a foot in diameter and many inches in thickness, concealing kidneys, bladder, and spermatic cords. In such cases, when one of the vessels of the varix is pricked or ruptures, the contents are found to be white or pinkish. They are not limpid like ordinary lymph. They are chyle, therefore; chyle on its way to enter the circulation by a retrograde compensatory track. When the varix involves the integuments of the scrotum, the result is "lymph scrotum"; when most prominent in the groin, then a condition of glands is produced which I have called "varicose groin glands"; when the lymphatics of the bladder or kidneys are affected and rupture from over-distension, then chyluria is the result; when those of the tunica vaginalis rupture, then there is chylous dropsy of that sac—"chylocele"; the same may happen in the peritoneum—chylous ascites. Occasionally varicose lymphatic glands, resembling those frequently encountered in the groins, are found in the axilla. Occasionally, also, limited portions of the lymphatic trunks of the limbs are similarly and temporarily, or more permanently distended. This, doubtless, is the pathology of all those forms of filarial disease characterised by visible varicosity of lymphatics, with or without lymphorrhagia.

Filariæ may disappear from the blood in such cases.—In filarial disease associated with lymphatic varix, microfilariæ are generally present in the blood as well as in the contents of the dilated vessels. Sometimes, it is true, the microfilariæ are not found. Such cases are probably of long standing; had the microfilaria been looked for at an earlier stage of the disease, it would probably have been discovered. I have watched cases in which the larva has disappeared in this way; though at first found in abundance in the blood, after a year or longer it ceased to appear there. The reason for this disappearance is doubtless the death of the parent parasites, an occurrence I have seen associated with attacks of acute lymphangitis. Although the original cause of the varix may thus disappear, the effect is permanent.

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Pathology of elephantiasis arabum.—*Microfilariæ not usually present in the blood in elephantiasis.*—In those cases of filarial disease in which elephantiasis arabum is the leading feature, it is not usual at any stage of the established disease to find microfilariæ in the blood or elsewhere, unless it be in countries in which filariasis is extremely common and reinfection, or extensive infection, highly probable.

Reasons for regarding elephantiasis as a filarial disease.—From this circumstance—the absence of microfilariæ from the blood in elephantiasis—the question naturally arises, Why attribute this disease to the filaria? The answer to this is: (1) The geographical distribution of *Filaria bancrofti* and of elephantiasis arabum correspond; where elephantiasis abounds there the filaria abounds, and *vice versâ*. (2) Filarial lymphatic varix and elephantiasis occur in the same districts, and frequently concur in the same individual. (3) Lymph scrotum, an unquestionably filarial disease, often terminates in elephantiasis of the scrotum. (4) Elephantiasis of the leg sometimes supervenes on the surgical removal of a lymph scrotum. (5) Elephantiasis and lymphatic varix are essentially diseases of the lymphatics. (6) Filarial lymphatic varix and true elephantiasis are both accompanied by the same type of recurring lymphangitis. (7) As filarial lymphatic varix is practically proved to be caused by the filaria, the inference that true elephantiasis—the disease with which the former is so often associated and has so many affinities—is attributable to the same cause, appears to be warranted.

Explanation of the absence of microfilariæ in the blood in elephantiasis.—If the filaria be the cause of tropical elephantiasis, how account for the absence of filaria larvæ in the blood, as is the case in the vast majority of instances of this disease? The answer to this is:—Either the disease-producing filariæ have died; or the lymphatics draining the affected area are so effectually obstructed by the filaria, its products, or its effects, that any microfilariæ they may

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contain, or may have contained, cannot pass along these vessels to enter the circulation.

We have already seen that in filarial lymphatic varix the parasite which produced the disease may die, particularly during attacks of lymphangitis; the same may occur in elephantiasis, and I believe that this does happen. I do not think, however, that this is the entire explanation.

Lymph stasis produced by filaria ova.—I have twice in filariasis found ova of the filaria in lymph; once in the lymph from a lymph scrotum, once in lymph procured by aspirating a varicose groin gland. Therefore, at times, the filaria may produce ova instead of swimming larvæ. The ova of the filaria are not like the long, supple, slim, active, swimming larvæ; they are passive, more or less rigid oval bodies nearly five times the diameter of the embryo coiled up in their interior. In consequence of their size and passive character the ova, unlike the normal free-swimming larvæ, are quite incapable of traversing such lymphatic glands as, in the event of their escape from the parental worm, they may be carried to passively by the lymph stream. It is an accepted fact in pathology that an essential element in the causation of elephantiasis is lymph stasis. I have ventured to conjecture that the stasis of lymph which eventuates in *tropical* elephantiasis is produced by embolism of the lymphatic glands by ova of the filaria.

If ova are expelled by the parent filaria, it must be as a result of some hurrying of the process of filarial parturition. That this does occur sometimes the discovery, already mentioned, of filaria ova in the lymph fully proves. We can readily understand how, in consequence of mechanical injury, to which from her exposed position in the limbs she must be frequently subjected, or of some other cause, the parent filaria may miscarry. Should this happen, then the contents of her uterus will be expelled prematurely, and before the ova, normally lying at the upper part of her uterus, have become the long, outstretched, active larvæ we see in the blood.

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If a crowd of these passive, massive ova are carried by the lymph stream to the lymphatic glands of a limb, in the lymphatic trunks of which a female filaria is lying aborting, embolism of the afferent lymphatics of the glands must result and stasis of lymph in the limb ensue.

Inflammation necessary for the production of elephantiasis.—Lymph stasis alone does not produce elephantiasis; this has been proved by experimental ligature of lymphatic trunks. It may produce a form of œdema, but not true elephantoid hypertrophy. Should inflammation occur in an area of lymphatic congestion so produced, as it is very apt to do on the slightest injury, then elephantiasis will supervene; for, unless the lymphatics of an inflamed area are patent, the products of inflammation are not completely absorbed. Erysipelatoid inflammation, frequently recurring, is a well-recognised feature of almost every case of elephantiasis arabum.

Sequence of events in elephantiasis.—The sequence of events in the production of elephantiasis is, I believe, as follows:—Parent female filaria in the lymphatic system of the affected part; injury of the filaria; premature expulsions of ova in consequence of injury; embolism of lymphatic glands by ova; stasis of lymph; lymphangitis from subsequent traumatism or other cause (as septic infection) in the congested area; imperfect absorption of the products of inflammation; recurring attacks of inflammation leading to gradual, intermittently progressive, inflammatory hypertrophy of the part.

In this way I explain the production of elephantiasis by the filaria. And in this way I explain the absence from the blood of the larvæ of the parasite which started the disease; they cannot pass the occluded glands. Very likely the parent worm dies at an early stage of the disease, killed by the cause which led to premature parturition, or by the subsequent lymphangitis.

The subjects of elephantiasis less liable than others to microfilariæ in the blood.—Some years ago I made a curious observation which supports the view just

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stated. I received from Surgeon-Major Elcum eighty-eight slides of night blood from eighty-eight natives of Cochin. Of these eighty-eight persons, fourteen were affected with elephantiasis, seventy-four were not so affected. Of the slides coming from the seventy-four non-elephantiasis cases, twenty contained microfilariæ, about one in every three and a half; of the fourteen elephantiasis cases, only one had microfilariæ. Why should the elephantiasis cases have proportionately fewer microfilariæ than the non-elephantiasis cases? The answer may be, that in the former the existence of elephantiasis implied that a large area of their lymphatic systems was blocked, and that the blood could be stocked with microfilariæ carried by the lymph from only a relatively small lymphatic area; and that there was, therefore, a proportionately lesser likelihood of the presence of parent filariæ having for their young an unobstructed passage to the blood.

FILARIAL DISEASES.

Enumeration of the filarial diseases.—The diseases known to be produced by *Filaria bancrofti* are abscess; lymphangitis; varicose groin glands; varicose axillary glands; lymph scrotum; cutaneous and deep lymphatic varix; orchitis; chyluria; elephantiasis of the leg, scrotum, vulva, arm, mamma, and elsewhere; chylous dropsy of the tunica vaginalis; chylous ascites; chylous diarrhœa, and probably other forms of disease depending on obstruction or varicosity of the lymphatics, or on death of the parent filariæ.

Abscess.—Occasionally, as already mentioned, whether in consequence of blows or other injuries, of lymphangitis, or of unknown causes, the parent filariæ die. Generally the dead body is absorbed, just as a piece of aseptic catgut would be. Sometimes the dead worm acts as an irritant and causes abscess, in the contents of which fragments of the filaria may be found. Such abscesses, occurring in the limbs or scrotum, will discharge in due course, or may be opened; they lead to no further trouble. Should they form in the thorax or abdomen, serious consequences and even death may ensue.

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Probably, in certain instances, abscess forms at times independently of the death of the parasite; *e.g.*, in varicose glands, in lymph scrotum, in elephantiasis.

The death of the parental filaria is apt to be lost sight of as a possible cause of abscess in the subjects of filarial infection. Deep-seated pain in the thorax or abdomen, with inflammatory fever followed by hectic, and a diminution in the number of microfilariæ in, or their entire disappearance from, the peripheral blood should, in such circumstances, suggest a diagnosis of filarial abscess and indicate exploration and, if feasible, active surgical interference.

Lymphangitis and elephantoid fever.—*Symptoms.*—Lymphangitis is a common occurrence in all forms of filarial disease, particularly in elephantiasis, varicose glands, and lymph scrotum. When occurring in the limbs the characteristic painful, cord-like swelling of the lymphatic trunks and associated glands, and the red congested streak in the superjacent skin, are usually apparent at the commencement of the attack. Very soon, however, the connective tissue and skin of the implicated area become inflamed and tense, and high fever, preceded by severe and prolonged rigor, sets in. The attack may continue for several days, and be accompanied by severe headache, anorexia, often vomiting, and sometimes delirium. After a time the tension of the inflamed integuments may relieve itself by a lymphous discharge from the surface. Usually the attack ends in profuse general diaphoresis. The swelling then subsides gradually though not entirely. Lymphangitis may be confined to groin glands, testis, spermatic cord, or abdominal lymphatics. When it affects an extensive abdominal varix, symptoms resembling peritonitis are rapidly developed and may prove fatal.

Diagnosis.—This fever, appropriately named by Fayrer "elephantoid fever," occurs habitually at varying intervals of weeks, months, or years, in nearly all forms of elephantoid disease. Its tendency to recur, the severe rigor ushering it in, and the terminal diaphoresis cause it to be mistaken

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for ague. In Barbados, where there is no malaria, it is habitually called "ague." The implication of the lymphatics, the local pain, the erysipelatoid redness and swelling, the prolonged pyrexial stage, the absence of the malaria parasite from the blood, the presence there very possibly of microfilariæ, and the powerlessness of quinine to control the fever, suffice for diagnosis. Nevertheless, error in diagnosis is common, particularly when the attacks recur frequently and with a certain degree of regularity, as is usually the case.

Treatment.—The treatment should consist in removing any cause of irritation, in rest, elevation of the affected part, cooling lotions or warm fomentations, mild aperients, opium to relieve pain, and, if tension is great, pricking or scarifying the swollen area under suitable aseptic conditions. Subsequently the parts, if their position permits, should be firmly bandaged.

Varicose groin glands (Figs. 86, 87).—Varicose groin glands are frequently associated with lymph scrotum, with chylous dropsy of the tunica vaginalis, or sometimes with chyluria. Occasionally all four conditions co-exist in the same individual.

Symptoms.—As a rule, commencing painlessly, the patient is not aware of the existence of these varicose glands until they have attained considerable dimensions. Then, a sense of tension, or an attack of lymphangitis, calls attention to the state of the groins, where certain soft swellings are discovered. These swellings may be of insignificant dimensions or they may attain the size of a fist. They may involve both groins, or only one groin; they may affect the inguinal glands alone, or the femoral glands alone, or, and generally, both sets together.

To the touch they feel soft, doughy, and obscurely lobulated. The skin, natural in appearance, can be glided over the surface, but the swellings themselves are not movable over the subjacent fascia. Occasionally hard, kernel-like pieces can be felt in their interior, or the entire mass may be more or less indurated. On thrusting a hypodermic needle into the swellings, white or reddish chylous, or clear

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lymphous fluid can be aspirated in abundance. This fluid coagulates rapidly and usually contains living microfilariæ.

Diagnosis.—It is important to be able to diagnose these tumours from hernia, for which they are often mistaken. This can be done by observing that they are not tympanitic on percussion; that though pres-

Fig. 86.—Varicose groin glands and chylocele. (*From a patient under the care of Mr. Johnson Smith.*)

sure causes them to diminish, they do so slowly; that there is no sudden dispersion accompanied by gurgling, as in hernia, on taxis being employed; that they convey a relatively slight or no impulse on coughing; that they slowly subside on the patient lying down, and slowly return, even if pressure be applied over the saphenous or inguinal openings, on the erect posture being resumed. The cautious use of the hypodermic

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needle will confirm diagnosis; which would be further strengthened by the co-existence of lymph scrotum, chyluria, or chylous hydrocele, and the presence of filariæ in the blood. *Chronic swellings about the groin, cords, testes, and scrotum in patients from the tropics should always be regarded as being possibly filarial.*

Pathological anatomy. — On dissection these tumours are found to consist of bunches of varicose

Fig. 87.—Varicose groin glands. (*From photo: Journ. of Trop. Medicine.*)

lymphatics, and to form part of a vast lymphatic varix involving the pelvic and abdominal lymphatics.

Treatment.—Unless they give rise to an incapacitating amount of discomfort, and are the seat of frequent attacks of lymphangitis, varicose groin glands are best left alone. It must always be remembered that they are part of an anastomosis necessary to life. Should they be very troublesome and incapacitate for work, they may be removed. In operating, strict

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aseptic methods must be practised, as septic lymphangitis readily occurs, and has frequently proved fatal in such cases. Excision is not always satisfactory, as it may be followed by lymphorrhagia at the seat of the wound, by excessive dilatation of some other part of the implicated lymphatic area, by chyluria, or by elephantiasis in one or both legs.

I have suggested that these tumours might be successfully treated by establishing an anastomosis between one of the dilated lymphatic vessels and a neighbouring vein. Mr. Godlee has twice performed such an operation for me with partial success. The operation is somewhat difficult, owing to the fragile nature of the dilated lymphatic vessels, and the shortness of their course.

It is said (Azema) that these glands tend to diminish in size after forty. I cannot confirm this statement from personal observation.

Similar varicose dilation of the axillary glands is sometimes, though much more rarely, found. Bancroft designated these varicose axillary and groin glands "helminthoma elastica."

Cutaneous and deeper lymphatic varices.—Occasionally cutaneous lymphatic varices are met with on the surface of the abdomen, on the legs, arms, and probably elsewhere. Sometimes they are permanent; sometimes, when more deeply situated, they constitute little swellings which come and go in a few hours. I believe these latter often depend on the actual presence of parent filariæ in the tumour. Such varices are evidence of lymphatic obstruction. Filarial lymphangiectasis of the spermatic cord is not uncommon. The contents may be milky and chylous, or straw-coloured and lymphous, according to situation and connections.

Thickened lymphatic trunks.—Maitland has frequently seen in Madras cases of lymphangitis in which, after the initial swelling and inflammation had subsided, a line of thickening remained. On excising this thickened tissue and carefully dissecting it, he has found minute cyst-like dilatations of the lymphatic involved, and in these cysts, coiled up, adult

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filariæ, sometimes dead, sometimes alive. The lymphangitis, he believes, is caused in these cases by the death of the filariæ. Daniels has made similar observations in British Guiana. Such a case I saw under the care of Dr. Abercrombie at Charing Cross Hos-

Fig. 88.—Lymph scrotum and varicose groin glands. (*From a photograph by Dr. Rennie, Foochow.*)

pital in London. On the subsidence of a filarial lymphangitis of the arm a thickening, about the size of a finger-tip, remained on the forearm. Believing that it contained adult filariæ, this thickening was excised by Mr. Young and placed in normal salt solution. Eight hours later the mass was carefully

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dissected, and a living female filaria, about four inches in length, was turned out. The parasite continued to live and swim about actively in the salt solution for nearly two hours.

Lymph scrotum (Fig. 88).—*Symptoms.*—In this disease the scrotum is more or less enlarged. Though usually silky to the touch, on inspection the skin presents a few, or a large number of, smaller or larger lymphatic varices which, when pricked or when they open spontaneously, discharge large quantities of milky, or sanguineous-looking, or straw-coloured, rapidly coagulating lymph or chyle. In some cases eight or ten ounces of this substance will escape from a puncture in the course of an hour or two; it may go on running for many hours on end, soiling the clothes of the patient and exhausting him. Usually microfilariæ can be discovered in the lymph so obtained, as well as in the blood of the patient. In a large proportion of cases of lymph scrotum the inguinal and femoral glands, either on one or on both sides, are varicose.

Probably provoked by friction against the thighs and clothes, erysipelatoid inflammation and elephantoid fever are frequent occurrences. Abscess is not uncommon. In time, in a proportion of cases, the scrotum tends to become permanently thickened and to pass into a state of true elephantiasis.

Treatment.—Unless inflammation be a frequent occurrence, or there be frequent and debilitating lymphorrhagia, or unless the disease is tending to pass into true elephantiasis, lymph scrotum—kept scrupulously clean, powdered, suspended, and protected—had better be left alone. Should, however, for these or other reasons, it be deemed expedient to remove the diseased tissues, this can be effected easily. The scrotum should be well dragged down by an assistant whilst the testes are pushed up out of the way of injury. A finger knife is then passed through the scrotum, and in sound tissues, just clear of the testes, and the mass excised by cutting backwards and forwards. No diseased tissues, and hardly

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any flap, should be left. Sufficient covering for the testes can be got by dragging on, and, if necessary, dissecting up the skin of the thighs, which readily yields and affords ample covering. It is a very common but a very great mistake to remove too little. As a rule, the wound, if carefully stitched and dressed antiseptically, heals rapidly.

In consequence of this sudden and violent interference with an extensive varix, of which that in the scrotum is but a part, chyluria, or elephantiasis of a leg, may supervene. The patient should be warned of this possibility.

Chyluria.—*Pathology.*—When a lymphatic varix in the walls of the bladder, or elsewhere in the urinary tract, the consequence of filarial obstruction in the thoracic duct, ruptures, there is an escape of the contents of the varicose lymphatics into the urine. Chyluria is the result.

Symptoms.—This disease frequently appears without warning; usually, however, pain in the back and aching sensations about the pelvis and groins—probably caused by great distension of the pre-existing lymphatic varix—precede it. Retention of urine, from the presence of chylous coagula, is sometimes the first indication of serious trouble. Whether preceded by aching, or by retention, or by other symptoms, the patient becomes suddenly aware that he is passing milky urine. Sometimes, instead of being white, the urine is pinkish or even red; sometimes white in the morning, it is reddish in the evening, or *vice versâ*. Sometimes, whilst chylous at one part of the day, it is perfectly limpid at another. Great variety in this respect exists in different cases, and even in the same case from time to time, depending on temporary closure of the rupture in the lymphatic, and also on the nature of the food.*

* The sanguineous appearance so frequently seen in chylous urine and in other forms of filarial lymphorrhagia probably depends in some instances on the formation of blood corpuscles in lymph long retained in the varicose vessels, and as a result of the normal evolution of the formed elements in that fluid; in other instances it is probably caused by rupture of small blood-vessels into the dilated lymphatics.

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Physical characters of chylous urine.—If chylous urine be passed into a urine glass and allowed to stand, as a rule, within a very short time, the whole of the urine becomes coagulated. Gradually the coagulum contracts until, at the end of some hours, a small, more or less globular clot, usually bright red or pinkish in colour, is floating about in a milky fluid. Later, the milky fluid separates into three layers. On the top there is formed a cream-like pellicle; at the bottom a scanty reddish sediment, sometimes including minute red clots; in the centre the mass of the urine forms a thick, intermediate stratum milky white or reddish white in colour, in which floats the contracted coagulum. If a little of the sediment be taken up with a pipette and examined with the microscope, it is found to contain red blood corpuscles, lymphocytes, granular fatty matter, epithelium and urinary salts, and, mixed with these in a large proportion of cases, though not in all, microfilariæ. The middle layer contains much granular fatty matter; whilst the upper cream-like layer consists of the same fatty material in greater abundance, the granules tending to aggregate into larger oil globules. If a small portion of the coagulum be teased out, pressed between two slides, and examined with the microscope, microfilariæ, more or less active, may be found in the meshes of the fibrine. If ether be shaken up with the milky urine, the fat particles are dissolved out and the urine becomes clear; the fat may be recovered by decanting and evaporating the ether which floats on the urine. Boiling the urine throws down a considerable precipitate of albumin.

Recovery and relapse.—Chyluria comes and goes in a very capricious manner. Sometimes the urine remains steadily chylous for weeks and months, and then suddenly, without obvious cause, becomes limpid and natural-looking, and free from fat or albumin. Later a relapse will occur, again to disappear after an uncertain time; and so on during a long course of years.

Retention of urine.—Retention of urine is not an unusual occurrence; it is produced by the formation

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of coagulum in the bladder. The retention usually gives way after a few hours of distress, worm-like clots being passed.

Constitutional effects.—Although chyluria is not directly dangerous to life, yet, being prolonged, it gives rise to pronounced anæmia, depression of spirits, and feelings of weakness and debility, and tends to incapacitate the patient for active, vigorous life.

Exciting causes of chyluria. — Chyluria is very liable to occur, either for the first time, or as a relapse, in pregnancy or after childbirth; the disturbance of the pelvic lymphatics in pregnancy and the muscular efforts attending labour apparently causing rupture of pelvic lymphatics previously rendered varicose by filarial obstruction of the thoracic duct. In men, running, leaping, and violent efforts generally are sometimes assigned as its cause; usually the exciting cause is not discoverable.

Treatment.—The treatment of chyluria should be conducted on the same lines as the treatment of inaccessible varix elsewhere; that is to say, by resting and elevating the affected part, and thereby diminishing as far as possible the hydrostatic pressure in the distended vessels. Many forms of medicinal treatment have been advocated. Because during treatment with some drug a chyluria has subsided, curative properties are apt to be attributed to the drug which was being taken at the time. The best results are got by sending the patient to bed, elevating the pelvis, restricting the amount of food and fluid—especially fatty food, gentle purgation, and absolute rest. It will be found that a day or two of treatment on these lines is often followed by temporary, perhaps prolonged, cessation of the chyluria. The drugs which have been particularly lauded in the treatment of this disease are gallic acid in large doses, benzoic acid in large doses, glycerine, the tincture of the perchloride of iron, decoction of mangrove bark, chromic acid, quinine, salicylate of soda, ichthyol, and *Nigella sativa*. I do not believe that these substances have any influence whatever in stopping the lymphorrhagia. Neither do I believe that thymol, recommended by

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Lawrie, or methylene blue, recommended by American writers, has any effect either on the filaria or on the disease it gives rise to; since their first recommendation both drugs have been tried, but in other hands have failed.

Filarial orchitis. — Several French writers describe under the name "malarial orchitis" a special form of inflammation of the testes, and here and there in Indian medical literature allusion is made to the same or a similar subject. I have many times seen filarial orchitis, but I cannot say I have seen orchitis of purely and unquestionably malarial origin. The fever attending filarial orchitis—which is usually associated with lymphangitis of the spermatic cord and perhaps with inflammation of the scrotum—like ordinary elephantoid fever resembles very closely a malarial attack, and may be mistaken for this. Without absolutely denying the existence of such a disease as malarial orchitis, I would suggest that the affection described by the French and Indian writers referred to, and endemic inflammations of testes, spermatic cords, and scrotum generally, are of filarial origin.

Filarial synovitis.—Maitland mentions acute synovitis of the knee-joint as one of the filarial diseases, and gives the particulars of five cases. He considers the concurrence of synovitis with filarial invasion too common to be accidental.

ELEPHANTIASIS.

Its prevalence.—Elephantiasis is by far the most frequent manifestation of filarial invasion, and is exceedingly common in some of the endemic districts. Thus, in certain districts in Cochin about 5 per cent. of the population, in Samoa about every second individual, in Huahine seven-tenths of the adult male population are affected. In many other tropical and sub-tropical countries, if not so common as in those just mentioned, elephantiasis is, nevertheless, common enough.

Parts affected.—In 95 per cent. of the cases the lower extremities—either one or both—alone, or in

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combination with the scrotum or arms, are the seat of the disease. The foot and ankle only, or the foot and leg, or the foot, leg and thigh, may, each or all, be involved. The scrotum is also a common situation for elephantiasis. The arms are more rarely attacked; still more rarely the mammæ, vulva, and circumscribed portions of the integuments of the limbs, trunk, neck, or scalp.

The recurring erysipelatoid attacks.—The disease in any of these situations commences with a rapidly evolved lymphangitis, dermatitis and cellulitis accompanied by elephantoid fever. On the subsidence of the acute symptoms the skin and subcutaneous fascia of the affected part do not quite resume their original proportions; the inflammatory effusion not being completely absorbed, some permanent thickening remains. Recurrences of this inflammation once or twice a month, or perhaps once in six months, or every twelve months, or even at longer intervals, add a little each time to the bulk of the limb or scrotum. Thus, gradually, an enormous swelling may be built up. Occasionally, though very rarely, enlargement may progress after one, two, or more initial inflammatory attacks, and without further recurrence of these.

Fig. 89.—Elephantiasis of the scalp. (*Journ. of Trop. Medicine.*)

Clinical characters of the swelling.—The affected part is greatly increased in bulk. The surface of the skin, in confirmed elephantiasis especially, is rough and coarse; the mouths of the follicles are sometimes unusually distinct; the papillæ and glands are either hypertrophied or atrophied; the hair is coarse and sparse; the nails are rough, thick, and deformed.

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Around joints the thickened integuments are thrown into folds, the comparatively smooth-sided and deep interlying sulci permitting limited movement. There is no distinct line of demarcation between healthy and diseased skin. The implicated integuments are hard, dense, pit but slightly if at all on pressure, and cannot be pinched up or freely glided over the deeper parts.

Its macroscopic anatomy.—On cutting into the swelling, the derma is found to be dense, fibrous, and enormously hypertrophied. The subjacent connective tissue is increased in bulk, having, especially in the case of the scrotum, a yellowish, blubbery appearance from lymphous infiltration. A large quantity of fluid wells out on division of such tissues. The muscles, nerves, and bones are not necessarily diseased, although in rare instances they may be degenerated and slightly or considerably atrophied from pressure. The blood-vessels are large; the lymphatics dilated; the associated lymphatic glands, both of the same side and very often of the opposite side, enlarged and dense.

True elephantiasis permanent.—Though in recent cases the bulk of the limbs may be much reduced temporarily by treatment, the disease is never permanently recovered from. Simple lymphatic œdema in areas which have never become inflamed subsides readily enough on pressure or elevation.

Elephantiasis of the legs (Fig. 90).—Elephantiasis of the lower extremities is usually, though by no means always, confined to below the knee. The swelling may attain enormous dimensions and involve the entire extremity, the leg or legs attaining a circumference, in aggravated cases, of several feet.

Treatment.—In the treatment of elephantiasis of the leg the patient should be encouraged to persevere with elastic bandaging, massage, and elevation of the limb. Castellani claims good results from a combination of these measures with daily injections of fibrolysin 2 c.c. Ligature of the femoral artery has been practised; it is probably useless, and is certainly not a

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justifiable method of treatment. Sometimes, in extreme cases, good results are got from excision of redundant masses of skin, a longitudinal strip of three or four inches in breadth by a foot or more in length being dissected off. Charles advocates complete resection of the whole of the elephantoid tissue except the sole of the foot, followed by extensive skin

Fig. 90.—Elephantiasis of legs; scrotum and right arm also affected. (*From a photograph by Dr. Turner, Samoa.*)

grafting. Electrolysis and mercury have also been used; I question their value. During the acute attacks, tension may be relieved by aseptic punctures with a sharp lancet. At all times the limb must be carefully guarded from injury, and shoes and trousers worn. Slight injuries provoke the inflammatory recurrences. Wading in water, prolonged standing, violent exercise, and exposure to a hot sun are injurious, and should be avoided.

Handley has recently brought forward an opera-

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tion, lymphangioplasty, the underlying principle of which is the drainage of an area of lymph stasis into an adjacent patent lymphatic area by means of strands of silk passing from one to the other. He describes the operation thus:—"Eight stout silk threads were led upwards from the foot to a point in the iliac

Fig. 91.—Elephantiasis of the scrotum; left leg slightly affected. (*From a photograph by Dr. Turner, Samoa.*)

fossa just above Poupart's ligament. These were spaced out round the limb at intervals. Above they united to form a leash. The iliacus muscle was exposed by a short incision like that for ligature of the external iliac artery. Half the threads were passed through a portion of the iliacus muscle, and were knotted in pairs to the other four threads, thus fixing

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them securely to the tissues of the iliac fossa. The multiple small incisions through which the threads were introduced were closed by horsehair sutures, leaving the silk completely buried in the subcutaneous tissues." He claims a comparative success in one marked case of elephantiasis of the leg. Judging from the narrative of this case (*Trans. Soc. of Trop. Med., Vol. II., p.* 41) the operation is attended with considerable risk from sepsis.

Elephantiasis of the scrotum (Fig. 91) *Weight of tumours.*—Elephantiasis of the scrotum, or "scrotal tumour" as it is sometimes called, may attain an enormous size. Ten, fifteen, or twenty pounds are common weights for these tumours, and forty or fifty pounds is by no means uncommon. The largest recorded weighed 224 lbs.

Anatomical characters.—There are certain points in the anatomy of scrotal tumour which the operating surgeon must bear in mind. These tumours consist of two portions (Fig. 92): first, a dense rind of hypertrophied skin (A *e*), thickest towards the lower part and gradually thinning out as it merges above into the sound skin of the pubes, perineum and thighs; second, enclosed in this rind, a mass of lax, blubbery, dropsical, easily torn through, areolar tissue in which testes, cords, and penis are embedded. The shape of the tumour is more or less pyriform. The upper part, or neck, on transverse section (B) is triangular, the base (B *k*) of the triangle being in front, the apex (B *j*)—usually somewhat bifid from dragging on the gluteal folds—towards the anus, the sides (B *k*) towards the thighs. In the latter situation the skin, though usually more or less diseased, is, from pressure, softer and thinner than elsewhere, tempting the surgeon to utilise it for the formation of flaps—not always a wise proceeding. The penis (A *a*, B *f*) always lies in the upper and fore part of the neck of the mass; it is firmly attached to the pubes by the suspensory ligament. The sheath of the penis is sometimes specially hypertrophied, standing out as a sort of twisted ram's horn-like projection on the anterior surface of the tumour; this however, is unusual. Generally the sheath of the penis is incorporated in the scrotal mass, the prepuce being dragged on and inverted so as to form a long channel leading to the glans penis and opening (A *l*) half-way down, or even lower, on the face of the tumour. The testes (A *c*) buried in the central blubbery tissue, usually lie towards the back of the tumour, one on each side, in large tumours generally nearer the lower than the upper part. They are more or less firmly attached to the under part of the scrotum by the hypertrophied remains of the gubernaculum testis (A *d*); a feature to be specially

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borne in mind by the surgeon. As a rule both testes carry large hydroceles with thickened tunicæ vaginales. The spermatic cords also (A *b*, B *g*), are thickened and greatly elongated. The arteries supplying these enormous growths are of considerable size; the veins, too, are very large, and, as they permit regurgitation of blood from the trunk, are apt to bleed freely.

Their importance.—Beyond inconvenience from their weight, the presence of the cumbersome mass between the legs, the suffering attendant on recurring attacks of inflammation and elephantoid fever, the sexual disability, and the unsightliness, these tumours are not of great importance: they do not as a rule, directly endanger life. They may grow rapidly or slowly; they may attain a large size in two or three years, or they may be in existence for years and at the end of this time amount to little more than a slight thickening of the scrotum. Occasionally, in large tumours, portions of the mass become gangrenous, or abscess may form, and in this way life may be endangered; this is not usual, however.

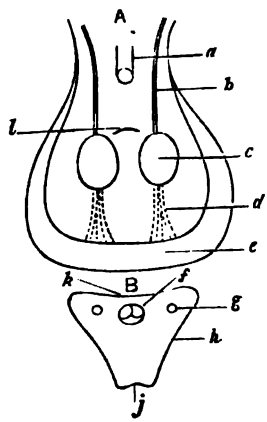

Fig. 92.—Diagram of the anatomy of elephantiasis of the scrotum.

Treatment.—Scrotal tumour, as soon as it becomes unsightly or inconvenient, should be removed. Often after thorough removal of all the diseased integuments, elephantoid fever, which before may have been frequent, ceases to recur.

Treatment preliminary to operation. — If the tumour is of considerable size, the patient should keep his bed for a day or two before operation, the mass being suspended so as to drain it of fluid and blood. It is thus rendered lax, and the operator is enabled to ascertain by palpation the position of the testes and, if such chance to be present, of hernia—a not very unusual complication. The possibility of undescended testes should not be overlooked.

Operation.—Before making provision for the prevention of hæmorrhage the operator should mark out

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by shallow cuts the line at which he proposes to separate the tumour, care being taken that these guiding incisions run through and include only absolutely sound skin. If the latter precaution be neglected, disease is very liable to recur in the scar or flaps. First, the tumour is turned up and a shallow transverse cut is drawn in sound skin across the perineum in front of the anus. The tumour being allowed to fall down, a similar shallow cut is made across the pubes. The corresponding extremities of these two

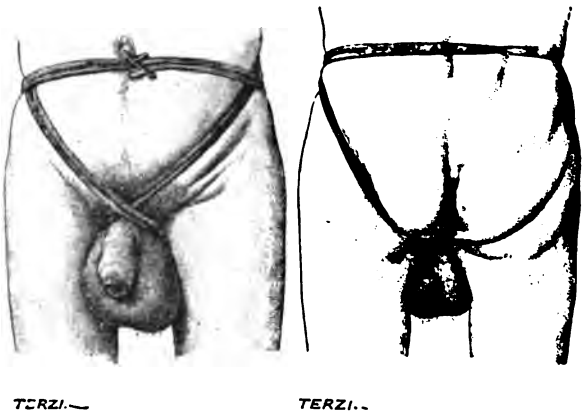

Fig. 93.—Rubber cord in position (McLeod).

cuts are then united either by a straight cut, or, if there be a little sound skin on the thigh aspects of the tumour, by semilunar incisions.

Assistants then firmly draw down the scrotum as far as possible, and the surgeon, if he deem it desirable, applies elastic webbing over the mass so as to expel the blood it contains. Next, a stout rubber cord is wound, figure of 8 fashion, round the neck of the tumour, well above the guiding incisions, and over the pelvis, and firmly secured (McLeod) (Fig. 93). Or the rubber cord is wound round the neck of the tumour only, being kept in place by four strips of

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bandage passing under this cord, one on each side of the scrotum before and behind, and firmly tied over another strip of bandage encircling the waist.

The testes and spermatic cords are first dissected out through long perpendicular incisions made in front, the remains of the gubernacula testes being hooked up with the finger and snipped through with scissors. The channel of the prepuce is next slit up, the incision being carried up to the pubic limiting mark. The penis can then be shelled out, the prepuce being first cut through around the corona glandis. If lateral flaps can be formed of sound skin they are then dissected up. The perineal and pubic incisions are now deepened and, assistants holding the testes and penis well out of the way, the neck of the tumour is cut through close to the perineum and pubes. Gaping vessels are all carefully ligatured, and redundant tunica vaginalis—if hydroceles be present—excised. The rubber cord is then removed.

When hæmorrhage has been controlled, the posterior halves of the flaps are brought together by sutures, the anterior halves being united over the testes to the pubic cut. The penis will therefore emerge from the point where the horizontal line meets the perpendicular line of what is now a T- or Y-shaped wound. If no flaps have been made, the testes may be fixed by stitching any tag of tissue connected with them to the perineum, and the dimensions of the wound reduced as much as possible by stitching up the corners at the pubes and perineum.

In dressing it is of importance that the raw surfaces be covered by some aseptic *non-fibrous* protective —such as oiled silk—before the antiseptic dressing is applied. A fibrous dressing next the raw surfaces is troublesome, as it sticks to the wound and is painful and difficult to remove. The dressing should be massive, well padded, and kept in place by an eight-tailed bandage secured in front and behind to a strap round the waist, a hole being cut in front for the penis to emerge. The large wound generally does well. Skin grafting should be practised freely and early, especially round the root of the penis.

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Mortality from operation.—The mortality from these formidable-looking operations, if they are carefully done, is small, and need not exceed 5 per cent. The results are very satisfactory, as a rule, the functions of the organs being retained or restored.

Elephantiasis of the arms.—This is comparatively rare. Allowing for the differences between the upper and lower extremities as regards gravitation of fluids, the symptoms and pathology of elephantiasis of the arm are the same as those of elephantiasis of the legs. Beyond the judicious employment of massage and elastic bandaging, little can be done in the way of treatment.

Fig. 94—Elephantiasis of the labia majora. (*After Nuñez.*)

Elephantiasis of the vulva and mammæ.—Elephantiasis of the vulva (Fig. 95) and mammæ (Fig. 96) is still rarer. Where growth has become inconveniently large the diseased tissues should be removed. Instances are on record in which the integuments of the mammæ have become so thickened, heavy, and elongated that the organ has descended to the pubes and even to the knee. One such tumour weighed twenty-one pounds after removal. Tumours of the labia or of the clitoris, similarly, may attain a great size—eight or ten pounds, or even more.

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Fig. 95.— Elephantiasis of vulva
From a photograph by Dr. Walter H. B. Macdonald.)

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Fig. 96.—Elephantiasis of mammæ; left leg and foot also affected.

(From a photograph by Dr. Davies, Samoa.)

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Elephantiasis of limited skin areas. — Corney states that pedunculated elephantoid tumours, springing from the groin or from the anterior surface of the thigh, are not uncommon in Fiji. One such tumour which he removed weighed twenty pounds. Daniels has seen, both in Fiji and in Demerara, several cases of this description (Fig. 97). Silcock describes a pedunculated tumour of this nature which

Fig. 97.—Pedunculated groin elephantiasis.
(*From a photograph by Dr. Daniels.*)

he removed from the neck of an East Indian, and which weighed, after removal, thirty pounds. I have often seen limited areas of elephantoid thickening of the skin, particularly on the thighs. These conditions are easily dealt with by simple operations.

Chylous dropsy of the tunica vaginalis, and of the peritoneum chylous diarrhœa.—

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Chylous dropsy of the tunica vaginalis is not an unusual occurrence in the tropics. A fluctuating swelling of the tunica vaginalis, which does not transmit light, and which is associated possibly with lymph scrotum, with varicose groin glands, with chyluria, or with microfilariæ in the blood, would suggest a diagnosis of this condition. These collections of chylous fluid in the tunica vaginalis generally contain enormous numbers of microfilariæ. They may be treated as ordinary hydroceles, either by aseptic incision or by injection.

Filarial orchitis with effusion into the tunica vaginalis, according to Maitland, is best treated by incision of the tunica vaginalis, turning out any clot that may be found in the sac, and stuffing the latter with iodoform gauze. This procedure, he says, gives immediate relief.

Chylous dropsy of the peritoneum and chylous diarrhœa of filarial origin are very rare.

Prophylaxis of filarial disease.—The prevention of filarial disease resolves itself into protection from mosquito bite. With this in view, unprotected wells, tanks, or stagnant pools must not be permitted in the neighbourhood of dwelling-houses. The influence of these in spreading filarial disease has been ably demonstrated by Daniels in Demerara, and by Low in Barbados. All vessels used for storing water should be emptied at least once a week. The mosquito net is indispensable in filarial as well as in malarial countries.

The subjects of filariasis should be regarded as dangers to themselves and to the community and be compelled to sleep under mosquito nets.

FILARIA PERSTANS, Manson, 1891. (Plate v., Fig. 2.)

Geographical range.—This parasite is very common in the blood of the natives of large districts in West Africa. I have found it in natives from Old Calabar and from the basin of the Congo—both in the coast negroes and in those from the interior. Annett, Dutton, and Elliott report its presence in many places in Southern Nigeria, in Northern Nigeria, in Lagos, in the Gold and Ivory Coasts,

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in the Kroo Coast, and in Sierra Leone. Daniels informs me that he has found it in a native of British Central Africa, residing on the east side of Lake Nyassa. On the Congo in parts it occurs in half the population. Prof. Firket, of Liége, has confirmed this observation as regards the Congo district. Cook, Hodges, and Low have found the parasite to be extremely common in Uganda, where, in some districts, Low has found it in 90 per cent. of the population. Sometimes it occurs along with *mf. loa*, *mf. bancrofti*, and, in British Guiana, as stated, with *mf. ozzardi*, in the same individual. I have never found it in West Indian negroes, nor, in fact, in natives of any country except those of tropical Africa, and in the aborigines of Demerara. I have thrice found it in Europeans who had resided on the Congo.

Fig. 98.—Tail of adult F. perstans.

Its characters.—*Microfilaria perstans* observes no periodicity, being present in the blood both by day and by night. In this respect it resembles *mf. demarquaii* and *mf. ozzardi*; and like these, in size, shape, and anatomical detail, it differs very materially from *mf. bancrofti* and *mf. loa*. The number of microfilariæ in the peripheral circulation may vary considerably, but there is no marked difference between day and night. Their special seat of selection is not the peripheral blood, but that of the heart, lungs, aorta and other large vessels. They have not been found in the spleen, and only rarely in the liver and pancreas.

The larva in the blood measures, on an average, 0·2 mm. in length by 0·0045 mm. in breadth; but, as it possesses in a remarkable degree the power to elongate and to shorten itself, these measurements do not always apply. It is manifestly much smaller than *mf. bancrofti* and *mf. loa*, and is further distinguished from these microfilariæ by the entire absence of a sheath, and by the characters of its caudal end, which is invariably truncated and abruptly rounded off. The taper terminating in the tail extends through quite two-thirds of the entire length of the animal. Further, if the head be carefully observed with a high power,

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a fang can generally be easily seen—much more easily than the corresponding structure in *mf. bancrofti*—in constant play, shot out and retracted. The anterior gap in the central column of cells or V spot is about 0·03 mm. from the cephalic extremity. There is no marked tail gap. No hooked cephalic prepuce can be made out. Its movements also differ from those of *mf. bancrofti*, for it not only wriggles about, just as that parasite does, but it indulges from time to time in long excursions through the blood, moving freely all over the slide, locomoting in fact very much in the same way as *mf. bancrofti* does in the mosquito's stomach after it has cast its sheath.

Adult form.—The adult form, discovered by Daniels in Demerara Indians, and subsequently identified by myself as that of *F. perstans*, is, like *F. bancrofti*, a long, cylindrical, filiform nematode. The body is smooth, without markings, the mouth simple and unarmed. The tail in both sexes is peculiar and characteristic; it is incurvated, and the chitinous covering at the extreme tip is split up as it were into two minute triangular appendages, giving it a mitred appearance (Fig. 98). The adult female measures 70 to 80 mm. in length by 0·12 mm. in breadth. The head is club shaped and measures 0·07 mm. in diameter. The genital pore opens at 0·6 mm. from the head. The anus opens at the apex of a papilla situated in the concavity of the curve formed by the tail. The diameter of the tail just before termination is 0·02 mm. The male is smaller than the female; it measures 45 mm. in length by 0·06 mm. in breadth. The diameter of the head is 0·04 mm. Close to the opening of the cloaca there are four pairs of preanal and one pair of postanal papillæ. Two unequal spicules may sometimes be seen protruding from the orifice. So far the adult forms have been found only in the connective tissues at the root of the mesentery, behind the abdominal aorta, and beneath the pericardium.

Life history.—Very little is known of the life history of *F. perstans*. Although it has a wide geographical range, this filaria is everywhere limited in its topography to areas covered by dense forest growth and abounding in swamps. In Kavirondo, where the forest disappears and the land is covered with scrub and short grass, it is not found; likewise it is not found on the grassy plains of the highlands of British East Africa. Towns and cultivated areas are free from it. This peculiar limitation of its distribution would indicate an intermediary restricted to similar stations, certain Tabanidæ, for instance, or certain species of sylvan mosquitoes. In order to find the intermediary host of *F. perstans*, Low made numerous experiments with many different species of mosquitoes (*Culex fatigans, C. atratus, C. viridus, C. luteolateralis, C. quasigelidus; Anopheles argyrotarsis, A. costalis, A. funestus; Stethomyia nimbus; Zanthinosoma musica; Mansonia africana; Uranotænia cæruleocephala; Tæniorhynchus fuscopennatus*) and other blood-sucking insects (*Pulex irritans, Sarcopsylla penetrans,*

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Pediculus capitis and *P. vestimentorum*). These insects were either caught in the huts of infected persons, or they were reared from the larva and then fed on infected persons. After a certain time they were dissected, but, with one exception, the results were negative. In one isolated instance two developmental forms were seen between the thoracic muscles of a *Tæniorhynchus fuscopennatus* reared from the larva and fed on infected persons. Christy suggests that the true intermediary host of *F. perstans* is *Ornithodoros moubata*, a tick of the sub-family *Argasinæ*. He gives no evidence in support of this view, which is contradicted by the facts of geographical and topographical distribution.

Pathology.—So far as known, *F. perstans* has no great pathological importance; the presence of the adult parasites in the mesentery appears to cause little harm to the host.

MICROFILARIA DEMARQUAII, Manson, 1895. (Plate v., Fig. 4.)

In examining blood sent me by Dr. Newsam from natives of St. Vincent, West Indies, I found this microfilaria in several individuals—in 10 out of 152 examined. It resembled *mf. bancrofti* and *mf. loa* so far as shape is concerned, but differed from them in size, its average measurements being, according to Low, 0·2 mm. by 0·005 mm. It is sharp-tailed, has no sheath, and observes no periodicity, being present in the peripheral circulation both by day and by night. Its movements are very active; it can shorten or elongate itself, and not only wriggle about very actively, but travel from place to place on the fresh blood slide. Nothing is known of its life history or pathological bearings.

I have met with the same parasite in the blood of natives of St. Lucia, W.I., an observation confirmed by Galgey, Low, and St. George Gray. Low has also found it in the blood of natives of Dominica and Trinidad. Usually some eight or ten parasites are found in a preparation of ordinary dimensions; occasionally instances of high degrees of infection are met with, in which hundreds of microfilariæ can be counted on every slide. Its distribution is singularly limited, even in the endemic districts.

Galgey found five adult female filariæ in the omental tissues of a patient in whose blood *mf. demarquaii* had been discovered during life. No male was found.

These worms closely resembled the adult *F. ozzardi*, but, according to Daniels, exhibited structural differences, especially as regards the shape of the head and tail, which led him to conclude that they are specifically distinct. They measured from 65-80 mm. in length, by 0·21-0·25 mm. in breadth. The head has a diameter of from 0·09 to 0·1 mm. The mouth is terminal. The genital pore opens at 0·76 mm. from the head. The alimentary canal is nearly straight, and terminates in an anus which is subterminal. The opening of the anus is marked by a slight papilla. The tail is curved and rapidly diminishes in size just below the anal papilla. A marked cuticular thicken-

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ing covers the tip of the tail. The diameter near the tip of the tail, before its termination, is 0·03 mm. *F. demarquaii* is a thicker worm than *F. perstans*. It differs from *F. bancrofti* and *F. ozzardi* in the greater size of the head, in the smaller tail, and particularly in the marked cuticular thickening at the tip of the tail. This thickening is knobby, but the divisions are not so well marked as in *F. perstans*. The intermediate host has not been discovered. Low believes it to be a rare species of mosquito. It is quite possible that some of the minute, sharp-tailed filariæ (*F. ozzardi*) of British Guiana are the same species.

I have also found a minute, non-sheathed, sharp-tailed microfilaria in the blood of natives of New Guinea, closely resembling *mf. demarquaii*. Whether these various minute, sharp-tailed, non-sheathed embryos belong to one or to several species it is impossible to decide until the adult forms of each have been discovered and compared.

FILARIA OZZARDI, Manson, 1897.

Some years ago I received from Dr. Ozzard, British Guiana, a number of blood films prepared from aboriginal Carib Indians inhabiting the back-country of that colony. Although the negroes and other inhabitants of the littoral and settled districts of British Guiana are very subject to *F. bancrofti* and to elephantiasis, in none of the considerable number of slides of Carib blood from time to time received from Drs. Ozzard and Daniels have I once encountered *mf. bancrofti*. Daniels records an identical experience. I am assured by Dr. Ozzard that elephantiasis is unknown amongst these people. On examining the blood slides referred to, I discovered certain nematode larvæ with characters so peculiar that I suspected they represented at least one new species of blood worm, which I called, provisionally, *F. ozzardi*. At least half of the slides examined contained these parasites, some slides only one or two, other slides as many as forty or fifty.

In size and shape five out of six of the embryos resembled very closely *mf. perstans* (p. 644)—that is to say, they were blunt-tailed, had no sheath, and were very minute (0·173 to 0·240 mm. by 0·0043 to 0·005 mm., Daniels). But along with the blunt-tailed filariæ, and on the same slides, there occurred a sharp-tailed form, also very minute, and resembling *mf. demarquaii*. Drs. Ozzard and Daniels confirmed this discovery. Both of these observers have had abundant opportunity of examining these microfilariæ alive. They found that the sharp-tailed and the blunt-tailed worms behave in fresh blood on the microscope slide much in the same way that *mf. perstans* and *mf. demarquaii* do; that is, they wriggle about very actively, at the same time retracting, elongating, and locomoting in the blood.

Parental form.—For a time the relationship of these microfilariæ, both to each other and to *mf. demarquaii*, remained undetermined. Later Daniels found parental filariæ—male

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and female—at the *post-mortem* examinations of two Demerara Indians whose blood, during life, contained both blunt- and sharp-tailed larvæ. The mature worms, apparently numerous, were about three inches in length and very slender—about one-half the diameter of *F. bancrofti*. They were, therefore, not *F. magalhãesi* (p. 649). The head was somewhat club-shaped and showed no papillæ. The tail of the male was much coiled, and carried at least one long protruding spicule. These worms were found in one case in the mesentery and in the fat at the base of the mesentery; in the other "not only in mesentery and abdominal fat, but also in the subpericardial fat." The embryos *in utero*, Daniels stated, were all blunt-tailed. I had an opportunity of comparing these worms with unquestionable adult *F. perstans*. I found them to be identical. The peculiar bifid arrangement of the termination of the tail was quite characteristic of that parasite (p. 645).

Later, Daniels found at the *post-mortem* examination of a third aboriginal, in whose blood both the blunt-tailed (*F. perstans*) and the sharp-tailed microfilariæ had been found (and no others), a few adult *F. perstans* and, in addition, a female and portion of a male worm of quite a different species—presumably the parental form of the sharp-tailed larvæ. The two latter adult worms lay close together, and were believed to have been located in the subperitoneal connective tissues in the anterior abdominal wall. Except in the matter of the caudal extremity, which was slightly bulbous and without cuticular thickening, in size and structure they closely resembled *F. bancrofti*. Daniels has drawn up a table of the leading dimensions of the three species—*F. bancrofti*, *F. perstans*, and of this possibly new filaria for which I propose to retain provisionally the name *F. ozzardi*.*

TABLE OF LEADING DIMENSIONS.

	FILARIA BANCROFTI.	FILARIA PERSTANS.	FILARIA OZZARDI.
	Mm.	Mm.	Mm.
Length	85 to 90	70 to 80	81
Greatest thickness ...	0·20 to 0·26	0·120	0·210
Diameter of head	0·055	0·070	0·050
Diameter of neck	0·049	0·054	0·039
Distance from head—			
(1) Of vaginal outlet ...	0·710	0·600	0·710
(2) Of ovarian opening ...	0·920	?	0 850
Distance from tail of anal papilla	0·225	0·145	0·230
Termination of tail ...	Blunt, circular, not bulbous.	Slightly bulbous; covered by thickened cuticle prolonged into two triangular appendages.	Bulbous cuticle not thickened.

* It is probable that *F. ozzardi* will turn out to be the adult form of *F. demarquaii*. In this event the former name, in conformity to the rules of nomenclature, will have to be dropped.

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FILARIA MAGALHÃESI, R. Blanch., 1895.

Professor Magalhães describes two sexually mature filarial hæmatozoa, male and female, which were found lying in the left ventricle of the heart of a child in Rio de Janeiro. No information was received as to the nature of the disease of which the child died, nor had any examination of the blood been made during life. The parasites were cylindrical, capillary, opalescent, white, uniform in thickness except where the body tapered towards the tail and at the club-shaped oral end. The mouth was simple, circular, unarmed; the cuticle marked with fine transverse striations. The female worm measured 155 mm. in length by 0·7 mm. in diameter, the male 83 mm. in length by 0·4 mm. in diameter. The tail of the latter was provided with four pairs of preanal and four pairs of postanal papillæ, and two spicules. Manifestly this parasite is specifically distinct from *F. bancrofti* and the other blood worms described above. Nothing is known of its life history, nor of the associated pathology.

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CHAPTER XLI

I. PARASITES OF THE CIRCULATORY AND LYMPHATIC SYSTEMS (*concluded*)

SCHISTOSOMUM HÆMATOBIUM (Bilh.–v. Sieb.), 1852

Definition.—A chronic, endemic disease caused by *Schistosomum hæmatobium* (=*Bilharzia hæmatobia*, *Distomum hæmatobium*), giving rise to cystitis and hæmaturia, or to proctitis, or to other symptoms, and characterised by the presence of the ova of that parasite in the urine, or in the fæces, or in both.

History and geographical distribution.—The frequency of hæmaturia in the natives of Egypt, and in visitors to that country, has long been remarked. The explanation of this peculiar circumstance was supplied by Bilharz, who in 1851 discovered the cause in a peculiar trematode, which Cobbold proposed to name *Bilharzia*, in honour of its discoverer.

In 1864 Dr. John Harley recognised the characteristic ova in cases of hæmaturia from Natal. The disease has since been found in many other parts of Africa, more particularly along the eastern side of the continent as far south as Port Elizabeth. Balfour found it in the Soudan. According to Low it is very frequent in the natives of Uganda. In Egypt, judging from Bilharz's, Griesinger's, and Sonsino's *post-mortem* records, it is present in quite one-half of the population. It occurs also in Arabia, Syria, Persia, Mesopotamia, Cyprus, and Mauritius.

Ætiology.—*The parasite* (Fig. 99). *Schistosomum hæmatobium* is a bisexual trematode belonging to the family *Schistosomidæ*. The *male* is white, cylindroid, measuring 11 to 15 mm. in length by 1 mm. in breadth. It possesses an oral and a ventral sucker of about equal size and placed close together. The cylindrical appearance of the worm is

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produced by the ventral infolding of the two sides of what would otherwise be a flat body. By this infolding a gynæcophoric canal is formed, in which the female can be partially enclosed. The outer surface of the body is closely beset with small cuticular prominences. The *female* is rather darker in colour than the male, considerably longer (20 mm.), more filiform, her middle being usually infolded in the gynæcophoric canal referred to, whilst her anterior and posterior portions remain free. The genital openings of the sexes face each other, and are placed immediately posterior to the ventral sucker. The sexes live apart while young, but on reaching maturity the female enters the gynæcophoric canal of the male.

These parasites are found in the blood of the portal vein, in its mesenteric and splenic branches, and in the vesical, uterine, and hæmorrhoidal veins. They have also been found in the vena cava; Sonsino considers that, if searched for, they would probably be found elsewhere in the circulation. Their numbers vary considerably. Sonsino reports finding in one case forty; in another case Kartulis found 300 in the portal vein and its branches. Looss has seen the submucous tissue of the bladder so rich in worms that a pair could be found in every area of half a cm. square.

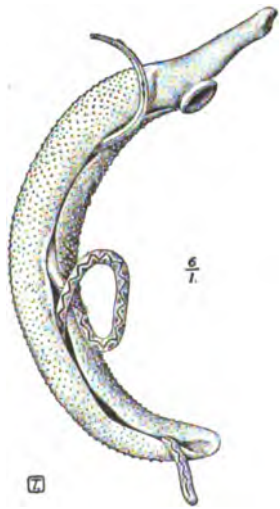

Fig. 99.—Schistosomum hæmatobium, male and female. (*Partly after Looss.*)

The ovum (Fig. 126, p. 705). — On microscopical examination the uterus of the female bilharzia is found to be stuffed with ova of a peculiar and characteristic shape. They are oval, each egg on an average measuring about 0·16 mm. in length by 0·06 mm. in breadth, and one end of the ovum is provided with a short, stout, and very definite spine.

The exact nature of the process by which the ova leave the body of the human host has not been satisfactorily explained. Apparently the female worm migrates from time to time from the larger veins to their smaller radicles, and in these deposits her ova. The walls of the bladder are the favourite situations for this purpose. Afterwards the eggs are somehow carried, possibly aided by the spine with which they are provided, towards the surface of the mucous membrane, and then,

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falling into the bladder, are voided with the urine, a certain amount of blood escaping at the same time.

The free larva (Fig. 102).—In newly voided urine the ovum presents a somewhat brownish appearance, and generally contains a ciliated larva (*miracidium*). After a time the larva may escape through a longitudinal rupture in the shell. It then swims about, but, unless supplied with fresh water, soon perishes. If the urine be freely diluted with water, the larva not only escapes more quickly from the shell but also continues to live, swimming and gyrating very actively for a considerable time. While swimming, the body of the little animal undergoes many changes of shape. For the most part, when advancing, it is oblong, tapering somewhat posteriorly; when more stationary it tends to assume a spherical form. It moves by means of the cilia which, with the exception of the

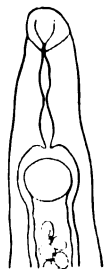

Fig. 100.—*Schistosomum hæmatobium*; anterior end of male. (*After Looss.*)

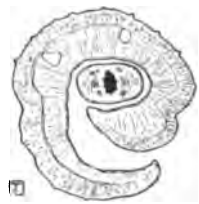

Fig. 101.—*Schistosomum hæmatobium*. Diagram of transverse section of male and female.

minute papillary beak, thickly cover the entire body. On carefully examining the larva, a canal may be traced from the beak into what looks like a rudimentary stomach; on both sides of this two much smaller gland-like organs can be seen, from each of which a delicate tube passes forward and opens, apparently, somewhere in the neighbourhood of the beak. The bulk of the larva is occupied by a number of sarcode globules. A careful description of the miracidium is given by Brock in the *Lancet* of Sept. 9th, 1893, p. 625, to which the reader is referred for further details.

Life history.—Beyond its first stage of free swimming ciliated larva, the extracorporeal life of schistosomum is quite unknown, notwithstanding the many attempts that have been made to trace its future progress. Sonsino believed at one time that he had discovered its intermediate host in a fresh-water arthropode; this view he afterwards abandoned. Analogy suggests that the miracidium passes into the body of some fresh-water mollusc, crustacean, or larval arthropode,

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there to undergo the developmental changes into redia and cercaria usually exhibited by the trematodes. Later, it may become encysted, and then, either free or still in the body of the intermediate host, gain access to man in drinking water, and so, through the stomach, pass to the veins of the portal system. Recently Looss has expressed the opinion that, unlike other trematodes, *Schistosomum hæmatobium* does not require the services of an intermediary host, and that the miracidium enters the human body directly by penetrating the skin. The natives of some parts of Africa believe that endemic hæmaturia is acquired in bathing, the parasite entering the body by the urethra, and, in consequence, employ various mechanical devices to prevent such a calamity. I would remark that if *S. hæmatobium* does not require the services of an intermediary host its peculiar geographical limitations are difficult to explain.

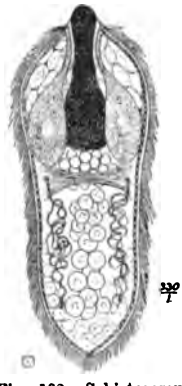

Fig. 102.—Schistosomum hæmatobium miracidium. (*After Looss.*)

Symptoms.—The symptoms produced by schistosomum vary in degree within very wide limits. In the vast majority of instances, the patient experiences no trouble whatever; in other instances the suffering is very great. Indirectly, from the serious nature of the lesions of the urinary organs to which it may give rise, schistosomum is an occasional cause of death.

The most characteristic symptom of its presence in the wall of the bladder is the passage of blood at the end of micturition, with or without a sense of urinary irritation. The quantity of blood passed and the degree of irritation are increased by exercise, by dietetic indiscretions, and by all such causes as are calculated to induce or aggravate cystitis. As a rule, it is only the last few drops of urine that contain blood; sometimes, however, the hæmorrhage is more extensive, and then the entire bulk of the urine may be blood-tinged. Occasionally, clots even are passed.

If in a case of moderate infection the urine be passed into a glass and held up to the light, minute flocculi, or coiled-up mucoid-looking threads, will be

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seen floating about in the fluid. If it be allowed to stand, the flocculi, and perhaps minute clots, will subside to the bottom of the vessel; these, on being taken up with a pipette and placed under the microscope, will be found to contain, besides blood corpuscles and the usual catarrhal products, large numbers of the characteristic spined ova.

In doubtful cases, where ova are few, the best way to find them is to get the patient to empty the bladder and to catch in a watch-glass the last few drops of urine which can be forced out by straining; these invariably contain ova. A low power of the microscope suffices, and is best for diagnosis.

Endemic hæmaturia lasts for months or years. Recovery is rarely complete. In ordinary cases, provided no reinfection take place, the hæmaturia tends to decrease, although ova may continue for years to be found in the last few drops of urine passed. In severe cases, sooner or later, signs of cystitis supervene and give rise to a great deal of suffering. Not unfrequently the ova become the nuclei for stone, and then symptoms of urinary calculus are superadded. Sometimes the pathological changes induced by the presence of the parasite in the bladder lead to the development of new growth, in which event the symptoms become more urgent and the hæmaturia perhaps excessive. Hypertrophy, contraction, and even dilatation of the bladder, are not unusual. Besides the bladder symptoms there may be signs of prostatic disease, or of disease of the vesiculæ seminales causing spermatorrhœa. In the latter case, ova may be detected in the semen. In other instances the ureters and kidneys become involved, and grave disease of these organs ultimately ensues. In consequence of the suffering which these aggravated forms of infection produce, the patients become

Fig. 103.—Section through nucleus of urinary calculus containing ova of Schistosomum hæmatobium.

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anæmic, wasted, debilitated, and a ready prey to intercurrent disease.

Milton has pointed out the extreme frequency of urinary fistula in Egypt, the result of schistosomum disease of the urethra. These fistulæ may occur anywhere in the neighbourhood of the genitals, but are especially common in the perineum and posterior surface of the scrotum, and originate from schistosomum disease of the pubic surface or roof of the urethra just in front of the bulb, the eggs of the parasite being deposited in the mucous or submucous tissue. Stricture of the urethra is by no means uncommon from a similar cause, especially in the case of fistulæ connected with the floor of the urethra.

Vaginitis and cervicitis have been known to be produced by this parasite. On the vulva papillomatous masses containing schistosomum ova are, according to Madden, very common.

Besides the lesions of the genito-urinary organs, rectal symptoms have been described and the characteristic ova of *S. hæmatobium* have been found in the rectum. Frequently, however, another species (*S. mansoni*), which invariably extrudes its eggs through the intestine, has been confounded with the old classic species. The intestinal lesions give rise to dysenteric-like symptoms. Very often mucus and blood are passed without any fæcal matter, and the continuous straining may be distressing, especially when large polypoid masses protrude from the anus. Recently I saw a case in which extensive condyloma-like growths around the anus, in the perineum and groin and full of ova, were a remarkable feature.

Pathological anatomy. — The character of the changes brought about by schistosomum varies very much according to the degree and the duration of the infection. In almost every case of the Egyptian type of the disease the walls of the urinary bladder are early affected. All that may be apparent to the naked eye at this stage is a certain amount of injection of the small vessels of the mucosa vesicæ, and, according to Sonsino,

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certain exceedingly minute vesicular or papular elevations of the surface of this membrane. When these minute elevations are examined microscopically they are found to contain ova. Ova are also to be found in the dilated minute blood-vessels. Later, especially in the trigone of the bladder, there are found rounded patches of inflammatory thickening which project somewhat, are granular on the surface, and dense in consistence; on section they creak under the knife as if they contained gritty particles. It is evident that these elevated, thickened patches are the result of an inflammatory process provoked by the clusters of ova which the microscope reveals scattered throughout their entire extent. The ova are principally deposited in the submucosa, less extensively in the mucous membrane itself, still less abundantly in the muscular walls of the organ or in its subserous connective tissue. They tend to occur in groups, each of which is invested with a sort of connective-tissue capsule; or they may be lying in small blood-vessels which they occlude. Some ova are seen to have undergone calcification; others are still fresh, either segmenting, or already containing a miracidium. On the surface of the rounded patches already mentioned, phosphatic deposits, also containing ova, are not uncommon; sometimes the patches present minute sloughs. In addition to these indurated patches, various forms of polypoid excrescence—sometimes ulcerated—may protrude from the mucous surface into the cavity of the bladder. These various hyperplasiæ frequently contain the adult parasite as well as ova.

In addition to what may be designated the specific changes in the mucosa, the muscular coats of the bladder are generally hypertrophied. In consequence of this, as well as of the ingrowth of villosities and different forms of new growth, the capacity of the organ may be much diminished. Its mucous surface is generally coated with a sanguineous mucus containing myriads of ova. Gravel, or small stones—generally phosphatic—are sometimes found either embedded in lacunæ in the hypertrophied and roughened bladder wall, or free in the

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cavity. Not unfrequently a similar hyperplasia occurs in the ureters, particularly towards their lower ends. In rare instances the pelvis of the kidney itself is affected. Obliteration of the ureter, both from small stones and, also, from thickening of the mucous membrane, has sometimes been met with; this leads to dilatation of the pelvis and atrophy of the parenchyma of the kidney. It is easy to understand how, in time, these changes of the bladder and ureters may give rise to hydronephrosis, pyelitis, abscess of the kidney, and similar secondary affections.

Hyperplasia from schistosomum infection may also occur in the vesiculæ seminales, in the walls of the vagina, and in the cervix of the uterus, leading to corresponding bloody, ova-containing discharges.

When the intestinal tract is involved numerous polypoid adenomatous growths are found, especially in the rectum; these usually slough off, leaving ulcerations with ragged edges. The coats of the gut become thickened and indurated owing to extensive fibrous tissue formation between the layers of the peritoneal attachments.

It may be mentioned that schistosome ova in small numbers have been found in the liver, in gall-stones, in the lungs, in the heart, and in the kidneys. We have no knowledge of any definite pathological change entailed by their presence there.

Tumours of schistosomum origin have sometimes been found in connection with the peritoneum and ligaments of the uterus.

Diagnosis.—The diagnosis of schistosomum disease is easy; the presence of ova in the urine is decisive. In countries like Egypt, where the disease must often concur with chyluria, with stone, with vesical tumour, with gonorrhœal cystitis, and with pyelitis, as well as with prostatic disease, care must be exercised in each particular case to separate the special factors to which the various symptoms are attributable. Thus in chyluria concurring with schistosomum disease there will be chyle in the urine in addition to blood. In such a combination the clot which forms will be large, will contain oil granules and globules and, very probably,

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microfilariæ, in addition to schistosomum ova; moreover, the microfilaria will generally be detectable in the finger blood if looked for at night. Stone in the bladder, when suspected, has to be searched for with the sound. In gonorrhœal cystitis the history of gonorrhœa will be forthcoming. In prostatic disease, enlargement of this organ may be made out. Difficulty may sometimes arise when ova are few in number, or when they have ceased altogether to come away in consequence of the death of the parent worms. The mischief wrought by the parasite remains, although the ova—the most certain evidence of the parasite's previous presence—may be discharged no longer. But, even if ova are very few, they may still be found in the last drop or two of urine passed. If they are no longer to be found in the urine, sometimes, by scratching the surface of the bladder with a sound and examining the shreds of mucus so obtained, a few, calcified it may be, but presenting the characteristic spine, may be seen with the microscope.

In rectal disease, if schistosomum be suspected, the mucus and fæces, or failing these one of the adenomatous growths, after removal by finger or forceps, should be examined for ova.

Prognosis.—An important element to be considered in venturing on a prognosis is the long life of the parasite. Sonsino mentions a case in which living ova were still being passed nine years after their first appearance, and after all chance of reinfection had ceased. Another important element in prognosis is the degree of infection; the greater the number of worms the more severe and the more extensive the disease they produce. As with filarial infection, the greater the number of cases in a district the greater the proportionate probability of severe infections being met with. The prognosis is practically that of a chronic cystitis depending on an irremediable, but not in itself fatal, cause. Much suffering may often be produced, and, as a consequence, anæmia and debility; possibly calculus may be formed; possibly grave renal disease may ensue; possibly villous or

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epitheliomatous growths in the bladder. In the milder degrees of infection, which fortunately are the commonest, the patient seems to be in no way inconvenienced by the parasite, and generally escapes all serious consequences. In any case, mild or severe, there may be attacks of hæmaturia from time to time; as a rule, the quantity of blood lost is insignificant.

Treatment.—Our knowledge of the situations occupied by the parasite indicates the futility of attempting a radical cure by means of poisonous substances, whether introduced by the bladder, by the rectum, or by the stomach. As yet we know of no direct, or other, means by which the schistosomes can be destroyed. Harm only can result from attempts at a radical cure of endemic hæmaturia on such lines. Our efforts must, therefore, be confined to palliating the effects of the presence of the parasite. Practically, the treatment resolves itself into that of chronic cystitis. The diet should be bland but nutritious; stimulants and spices are to be avoided. Excess of all kinds, violent muscular efforts, cold and other causes of catarrh must also be guarded against. During exacerbations of hæmaturia, or of cystitis, rest should be enjoined and diluents freely partaken of. Milton has obtained good results from gramme doses of extract of male fern three times a day in schistosomum hæmaturia. A recent writer has advocated the use of methylene blue (3 grs., three times a day) in similar circumstances. Adrenalin has some influence in controlling hæmorrhage. Pain may demand anodynes. Excessive catarrh of the bladder suggests washing out with weak boric acid lotion, and the internal administration of urotropine, uva ursi, buchu, perhaps small doses of cubebs, copaiba, or sandalwood oil, salol, benzoic acid, and so forth. Stone, and troublesome new growths, are to be removed by operation. Where distress was extreme, Mackie and others have had good results from perineal cystotomy and drainage. Adenomatous growths in the rectum, where accessible, should be removed. In severe rectal disease, milder measures failing, excision of the affected part of the gut may

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be necessary. Perineal fistula must be dealt with on ordinary surgical principles. Hyperplasia in the vagina and cervix is best treated by scraping.

Prevention.—Since analogy justifies the belief that the larva of schistosomum, on obtaining access to fresh water, enters a fresh-water animal and by it obtains access to another human host, it is evident that if the larva be kept from getting into the water, or, if drinking water be boiled or filtered, the spread of the disease from man to man would be effectually prevented.

In the endemic districts, children, in particular, should be carefully and repeatedly warned against drinking the water of ponds and canals. Provided reinfection be avoided by the exercise of prudence in the matter of drinking water, there is no necessity for sending the patient with schistosomum disease away from the country in which the parasite was acquired.

Every care should be exercised to prevent the diffusion of the disease, by prohibiting the evacuation of excreta into water where the miracidia might find the opportunity of development and transmission. This prohibition should not be restricted to patients, but extended to all, because, as special inquiries have shown, a large proportion of the infected do not suffer from any troublesome symptom, and are often unaware of the infection.

SCHISTOSOMUM MANSONI, Sambon, 1907.

The occurrence of a schistosomum producing lateral-spined ova was noticed by Bilharz in 1851, but he confounded it with *S. hæmatobium*, believing the lateral-spined ova to represent peculiar capsules formed by the larvæ after hatching. After Bilharz several observers encountered female worms with lateral-spined ova *in utero*, and the idea of a distinct species suggested itself to Sonsino and others, but this idea was at once discarded in favour of other hypothesis. The lateral-spined ova being found solely in the fæces of Egyptian patients suffering from hæmaturia, the majority of physicians held that the

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peculiar position of the spine was due to distortion of the egg-shell in passing through the muscular coat of the rectum, forgetting that oviposition takes place in the sub-mucous layer, and that lateral-spined ova are found in the uterus of the parent worm. Sonsino suggested that the two kinds of eggs might represent respectively male and female embryos. Looss surmised that the lateral-spined ova might be the product of unfertilised females.

In 1903, in examining a patient who had long resided in Antigua and other West Indian Islands and who had never visited Africa, I found in his fæces numerous schistosomum eggs all bearing a lateral spine. Repeated examination of the urine proved negative, and the patient stated that he had never at any time suffered from hæmaturia. This case, together with the absence of endemic hæmaturia in the West Indies, led me to think that probably the lateral-spined ova indicated a distinct species of schistosomum, and I suggested this in a previous edition of this manual and elsewhere. Since then a considerable amount of information has accumulated in favour of my conjecture. A new species of schistosomum (*S. japonicum*) with spineless ova, and affecting the intestine only, has been discovered in Japan, and careful examination for helminths in the Congo Free State (Bröden) and in Porto Rico (Gunn and others) have shown the absence of urinary schistosomum disease and the frequency in these regions of a rectal schistosomum infection in which the ova of the parasite bear invariably a lateral spine. Finally Sambon (*Proceedings of the Zoological Society*, March 9th, 1907), having had the opportunity of comparing specimens of the type characterised by lateral-spined ova with *S. hæmatobium* and other schistosomidæ, and taking into consideration its peculiar geographical distribution and distinct pathogeny, proposed that it should be ranked as a distinct species, and paid me the compliment of naming it *S. mansoni* in recognition of my suggestion.

The available material being very badly preserved, Sambon was unable to furnish the exact dimensions

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and the anatomical details of the new species, which closely resembles *S. hæmatobium* in general appearance and structure.* His determination is based chiefly on the egg characters. After stating that other species of animals, as for example an ostrich (*Rhea*), have been established solely on the characters of their eggs, Sambon calls attention to the fact that all the schistosomidæ of man and cattle are very much alike in general morphology, the only striking and characteristic difference being that of their ova, which differ markedly in each species. In *S. hæmatobium* the eggs are more or less ovoid and provided with a short straight terminal spine; in *S. bovis* they are spindle-shaped and provided with a short terminal heart-shaped spine; in *S. japonicum* they are ovoid and have no spine; and in *S. mansoni* they are oval and provided with a large thick lateral spine.

A careful comparative examination will probably show many structural differences between *S. hæmatobium* and *S. mansoni;* meanwhile that of the ova is sufficient in itself to separate the two species.† Apparently *S. mansoni* like *Necator americanus* is a West African species which has been introduced into the western hemisphere by the African negro.

S. mansoni inhabits chiefly the mesenteric veins, and its ova deposited within the sub-mucous layer of the rectum give rise to dysenteric-like symptoms, mucus with blood being passed from time to time, the ova-laden stools becoming frequent and their passage perhaps being attended with tenesmus. In such cases small, sometimes large, branching, soft growths are to be felt inside the *sphincter ani*. They resemble polypoid growths and are apt to be mistaken for piles. They may extend as high up the bowel as the sigmoid flexure. On tearing up one of these growths, the ova can be seen in the *débris*.

* In both species the males present a tuberculated outer surface, but the number and shape of the prominences seem to differ somewhat.

† Holcomb, in a paper just received, mentions five autochthon cases of intestinal schistosomum infection in the island of Vieques. The ova of the parasite were invariably lateral-spined. He states that 167 similar cases have been reported in Porto Rico; the eggs being found solely in the fæces, never in the urine.

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The eggs of *S. mansoni* have been found also in the liver, giving rise to a peculiar form of cirrhosis.

SCHISTOSOMUM JAPONICUM, Katsurada, 1904.

Synonym.—*Schistosomum cattoi*, Blanchard.

History.—For some years Japanese physicians had observed in the provinces of Yamanashi and Hiroshima in Central Japan, and at Saga in the north island, an endemic disease characterised by enlargement of the liver and spleen, cachexia and ascites. The patients suffered from diarrhœa, their motions containing mucus tinged with blood. Occasionally they had fever. They became anæmic, and many of them died from exhaustion. At the autopsy the liver and other organs were found to contain the ova of some unknown helminth.* In April, 1904, Katsurada discovered that the eggs found in the stools of these patients contained a ciliated embryo not unlike the miracidium of *Schistosomum hæmatobium*. Disappointed of an autopsy, he examined dogs and cats in the endemic area, and had the good fortune to find at once in the portal system of two cats from the province of Yamanashi numerous schistosomidæ containing eggs exactly similar to those previously found in man. He published this information on August 13th, 1904, and named the new trematode *S. japonicum*. Almost simultaneously, and independently, Fujinami observed cases of the disease in the village of Katayama in the province of Bingo, and found in his first fatal case the characteristic ova in various organs. In a second necropsy, besides the ova in the liver, intestinal wall and mesenteric glands, he found in a branch of the portal vein a parasite which he regarded as *S. hæmatobium*. In November, 1904, Catto discovered the same parasite in sections of the mesocolon from a Chinaman of the province of Fukien who died of cholera at St. John's Island, Quarantine Station, Singapore.

* As far back as 1888 Majima, in Tokio, found peculiar ova in the liver of a case of cirrhosis. These he described as the ova of an unknown parasite. In 1890, in a similar case, Yamagiwa found ova which he ascribed to the lung trematode.

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Description of the parasite.—*Schistosomum japonicum* closely resembles in general structure *S. hæmatobium*. As in the latter, the suckers are placed close together at the anterior extremity of the body, the acetabulum or posterior sucker being distinctly pedunculated and funnel-shaped. The suckers in both sexes and the ventral surface of the body in the male are provided with minute spines. The distinctive characters of the new trematode are its smaller dimensions (male 9 to 12 mm. in length by 0·5 mm. in breadth; female 12 mm. in length by 0·4 mm. in breadth), and the larger size of the acetabulum as compared to the oral sucker. In the male the integument is smooth and non-tuberculated, and the posterior part of the body in the male is relatively wider, the sides overlapping one another far more extensively than in *S. hæmatobium*. Finally, the ova (70 to 75 μ in length, 45 to 55 μ in breadth) are smooth and possess no spine. A comparative study of the anatomy of the two schistosomidæ will probably show other morphological differences. Catto mentions a larger vas deferens and lobular testicles in the male, and a different arrangement of the yolk cells in the female. Looss notices a greater development of the muscular system in the male *S. japonicum*, which he thinks may take the place of the want of cuticular eminences.

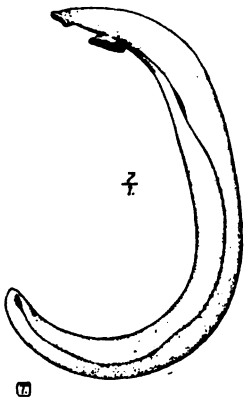

Fig. 104.—Schistosomum japonicum (male).

Catto found the adult worms in the smaller mesenteric blood vessels, but he was unable to determine whether they occupy the arteries or the veins. He believes they occur in both. The smooth, non-tuberculated skin of *S japonicum* seems to suggest a different anatomical habitat to that of *S. hæmatobium*, the integument of which is beset with numerous spine-bearing protuberances. *S. hæmatobium*, inhabiting the venous system, has a rough integument, it may be to enable it to adhere to the inner coat of the venules, and to stem the blood-stream during oviposition. *S. japonicum*, inhabiting the arteries, requires no integumental protuberances, the direction of the arterial current maintaining it in its proper position.

In Catto's case the ova were found chiefly in the mucous and sub-mucous coats of the intestinal tract from cæcum to anus, more especially in the rectum and appendix. They were also found in the liver, in the gall-bladder, in the pancreas, in the mesenteric glands, and in the fibrous coat of the larger

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mesenteric vessels. In the liver they were very plentiful, lying singly or in clusters embedded in the hypertrophied connective tissue. The female schistosoma probably has a special means of extruding her eggs through the walls of the blood-vessels; the further distribution of the eggs being affected by the lymph stream. Where the ova accumulate they provoke a small-cell infiltration, which gives place later to fibrous tissue.

Nothing is known of the life history of this trematode. Its ova contain a ciliated miracidium, which may develop in the fæces even before they are evacuated. The parasite, therefore, needs water during its miracidium stage, and, possibly, some freshwater mollusc or crustacean for further development.

Geographical distribution. — The distribution of *S. japonicum* is probably a wide one. So far it has been found only in Chinese and Japanese. In Chinese it has been found twice, once by Catto in a native from the province of Fukien, and once by Logan in a Chinaman from the province of Hunan. Catto suggests that the parasite was not recognised before probably because its ova in the stools were mistaken for those of *Ankylostomum duodenale*, which they resemble in size, shape, and general appearance.

Morbid anatomy.—Catto's patient during life presented enlargement of the liver and spleen. At the autopsy the appearance of the peritoneum suggested repeated attacks of peritonitis. The appendices epiploicæ were thickened, and in some places matted together. The recto-vesical pouch was almost obliterated. The mesenteric and prevertebral glands were enlarged, the largest group forming a cluster near the duodenum. The liver was considerably hypertrophied, its surface nodular, its consistence greatly increased. The coats of the gall-bladder were thickened, and a layer of fat almost completely encased this organ, which was distended with clear mucoid material containing several minute black gall stones. The spleen was enlarged and pigmented. The colon was much thickened throughout. Its mucous membrane was swollen, hyperæmic, and friable; it presented numerous small circular superficial erosions and patches of necrosis. The outer coats were very tough, almost cartilaginous. The

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walls of the rectum were three-quarters of an inch thick and adhered to the bladder. It nearly filled the true pelvis. The sigmoid flexure also was uniformly thickened. In tracing the bowel upwards the thickening became less marked and more patchy. The liver and bowel cut gritty on section. The bladder was thickened where adhesions had formed with the rectum, but elsewhere it was healthy, and nowhere was the vesical mucosa diseased. Sections of the liver, mesenteric glands, and bowel were found to contain the ova of *S. japonicum*.

In a case from Katayama, described by Tsunoda and Shimamura, the necropsy revealed, besides the ordinary lesions in the liver, intestine and pancreas, thickening, with hæmorrhagic infiltration of both the dura and pia mater. In the brain itself a number of wedge-shaped sclerosed areas of greyish colour, and surrounded by some ecchymosis, were found. In the lenticular nucleus, optic thalamus, and internal capsule of the left side there was an area of softening the size of a walnut. On histological examination these areas were found to contain ova embedded in neuroglia and surrounded by softened and degenerated brain tissue. Similar ova were found in the membranes and a few in the right hemisphere and in the choroid plexuses of the lateral ventricles. In connection with these lesions the patient during life suffered from disorder of speech and tremor in both upper and lower extremities, with headache and mental disturbance, later from vertigo and Jacksonian fits (two or three daily), and finally from right hemiplegia.

Katsurada has drawn attention to the fact that *S. japonicum* does not affect the bladder. The two cases described in Chinamen confirm this experience. These are, therefore, important pathological and clinical features which, in addition to the zoological characters of the parasites, show that *S. japonicum* is specifically distinct from *S. hæmatobium*.

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CHAPTER XLII

II.—PARASITES OF THE CONNECTIVE TISSUE

DRACUNCULUS MEDINENSIS; FILARIA LOA; FILARIA VOLVULUS

DRACUNCULUS MEDINENSIS, Velsch, 1674

Synonyms. — *Vena medinensis, Dracunculus persarum, Gordius medinensis, Filaria dracunculus, F. medinensis, Guinea-worm.*

Geographical distribution.—This important parasite is found in certain parts of India—the Deccan, Scinde, etc.—in Persia, Turkestan, Arabia, tropical Africa—particularly on the west coast, and in a very limited part of Brazil (Feira de Santa Anna). Formerly it was supposed to be endemic in Curaçoa, Demerara, and Surinam; apparently it has now disappeared from these places. Dracunculus is not equally diffused throughout this extensive area; it tends to special prevalence in limited districts, in some of which it is excessively common. In parts of the Deccan, for example, at certain seasons of the year nearly half the population is affected; and in places on the West Coast of Africa nearly every negro has one or more specimens about him. Although guinea-worm is sometimes seen in Europe, this is only in natives of or in recent visitors from the endemic area. Though frequently introduced in this way, it has not become established either in Europe or in North America. We have no account of the parasite as endemic in any part of Asia east of Hindustan, in the Eastern Archipelago, in Australia, or in the Pacific Islands.

Dracunculus medinensis has been reported for horses, oxen, dogs, wild cats, jackals, leopards and other animals. Possibly, some of the parasites in the

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lower animals described as guinea-worm may belong to quite a different species.

The parasite (Fig. 105).—The female is reputed to attain in some instances enormous dimensions; it is probable, however, that worms of five or six feet in length owe their size to errors of observation, two worms, or their fragments, having been regarded as one. According to Ewart, in forty carefully measured specimens the smallest was about 32·5 cm.,

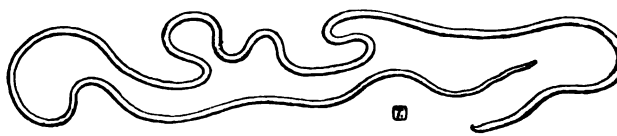

Fig. 105.—Dracunculus medinensis (reduced).

the largest 1 m. 20 cm. in length; 90 cm. is probably an average length. The diameter of the worm is about 1·5 to 1·7 mm. The body is cylindrical, milky-white, smooth, and without markings. The tip of the tail comes to a point and is abruptly bent, thus forming a sort of blunted hook, perhaps functioning as a "holdfast." The head end is rounded off, terminating in what is known as the cephalic shield. The mouth is triangular, very small, and surrounded by six papillæ—two large and four small. The alimentary canal is relatively small, being compressed and thrust to one side by the uterus; in the mature worm it is probably cæcal, for it has not been traced to an anus. Nearly the entire worm is occupied by the uterus, which is packed from end to end with coiled-up embryos. The vagina also may be lacking. According to Looss, the uterine tubes (he says, contrary to Leuckart, that there are two) open into the posterior part of the œsophagus by a common duct, the œsophagus prolapsing through the mouth at the time of parturition and being subsequently withdrawn. Leiper, however, has shown that the worm discharges its young by a prolapse of the uterus as described by me, and that the extrusion does not occur through the mouth, as suggested by Looss and myself, but by an opening just outside the circumoral ring of papillæ, possibly the vagina.

Fig. 106.—Dracunculus medinensis. (*After Leuckart.*)

Nothing definite is known of the male worm. According to Polak, the Persians have long known the male to be a smaller worm, 7-10 cm. long. They stated that at times

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as many as twenty of these small worms might be found coiled round a female specimen. Charles described a shorter (4 cm.) worm, regarding it as the male, which he found twice attached to the larger female worm within the sub-peritoneal connective tissue. Charles's description does not exclude the possibility that what he describes as the male worm *in coitu* was really a prolapse of the uterus through the ruptured integument. Daniels, at the *post-mortem* of a monkey experimentally infected by Leiper six months previously, found three immature females (30 cm. long) and two remarkably small males (22 mm.), which were obtained, one from the psoas muscle and the other from the connective tissue behind the œsophagus.

Habits.—The habitat of the female guinea-worm is the connective tissue of the limbs and trunk. When mature, and prompted by instinct, she proceeds to bore her way through this tissue, travelling downwards. In 85 per cent. of cases she presents in some part of the lower extremities. Occasionally she presents in the scrotum; rarely in the arms; very exceptionally in other parts of the body, or even in the head. In a proportion of cases the appearance of the worm at the surface of the body is preceded by slight fever and urticaria as described by Sutherland in 1897 and by Bartet independently in 1898. Arrived at her destination she pierces the derma. Probably in consequence of some irritating secretion, a small blister now forms and elevates the epidermis over the site of the hole in the derma. By-and-bye the blister ruptures, dis-

Fig. 107.—Transverse section of D. medinensis. (*Leuckart.*)

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closing a small superficial erosion half to three-quarters of an inch in diameter. At the centre of the erosion, which sometimes quickly heals spontaneously, a minute hole, large enough to admit an ordinary probe, can be seen. Sometimes, when the blister

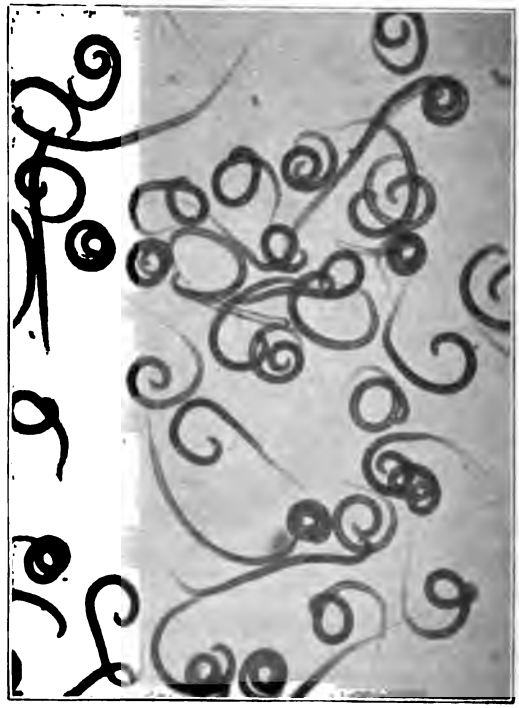

Fig. 108.—Embryos of D. medinensis.
(*From a microphotograph by Mr. H. B. Bristow.*)

ruptures, the head of the worm is seen protruding from this hole; as a rule, however, at first the worm does not show. If now we douche the neighbourhood of the ulcer with a stream of cold water expressed from a sponge and, as the water falls, watch the little hole in the centre of the erosion, we

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shall see in a few seconds a droplet of fluid—at first clear, later milky—well up through the hole and flow over the surface. Sometimes, instead of this fluid, a small, beautifully pellucid tube, about 1 mm. in diameter, doubtless the uterus of the worm prolapsed through her head parts, is projected through the hole in response to the stimulus of the cold water. When this tube has been extruded an inch or thereabouts, it suddenly fills with an opaque whitish material, ruptures and collapses, the fluid spreading over the surface of the erosion. If a little of the fluid, either that which has welled up through the hole, or that which has escaped from the ruptured tube, is placed under the microscope, it is seen to contain myriads of dracunculus larvæ lying coiled up, almost motionless, with their tails projecting in a very characteristic manner (Fig. 108). If now a drop of water be instilled below the cover-glass the larvæ may be observed to unroll themselves and, in a very short time, to swim about, *more suo*, with great activity. Manifestly these larvæ come from a guinea-worm lying in the tissues and communicating with the surface through the little hole in the derma. If the douching be repeated after an hour or longer a further supply of larvæ can be obtained; and this can be continued from time to time until the worm has emptied herself. Apparently the cold applied to the skin of the host stimulates the worm to contract and thereby force out her uterus, inch by inch, until it is completely expelled. When the protruded portion of uterus ruptures, under the pressure of the *vis a tergo*, it shrivels up, dries, and thereby effectually seals up the end of that part of the organ still inside the worm, thereby preventing what might be inopportune and too prodigal discharge of larvæ.

The larva (Fig. 109).—The larvæ are not cylindrical; they are distinctly flattened. In swimming they move by a sort of side-to-side lashing of the tail, and tadpole-like motion of the body. The movements are intermittent; sudden, short swims alternating with brief pauses. When progressing, the longer transverse axis of the body is perpendicular to the plane travelled over; but when, from time to time, the little worms pause they gradually roll over on to their flat surfaces. As

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soon as they come to rest on the flat they suddenly recover themselves with a jerk, and turn quickly on to their edges and begin swimming about again. This series of movements is constantly repeated.

The larva of *D. medinensis* measures about 0·50 to 0·75 mm. in length, by 15 to 25 mm. at its greatest breadth. The head is somewhat tapered and then abruptly rounded off. The tail is long, slender, but not quite sharply pointed. The alimentary canal can be readily detected. Towards the root of the tail two peculiar gland-like organs, placed opposite to each other, can be made out. The cuticle is very distinctly transversely striated.

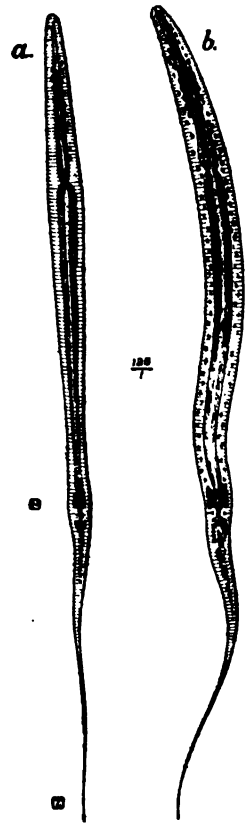

Fig. 109.—Embryos of D. medinensis.
a, Side view; *b* (*after Looss*), front view.

In clean water the larva remains alive for six days; in muddy water, or in moist earth, it will live from two to three weeks. If slowly desiccated it does not die; it may be resuscitated by placing it again in a little water.

Intermediary host. — If, by way of experiment, we place some dracunculus larvæ along with *Cyclops quadricornis* in a watch-glass we shall find that, after a few hours, the larvæ have transferred themselves to the interior of the body cavity of the cyclops, where they can be seen moving about, coiling and uncoiling themselves, with considerable activity (Fig. 110). As many as fifteen or twenty young guinea-worms may be counted in each of the little crustaceans, which, unless the infection is excessive, seem in no way inconvenienced. After a time, the embryos so transferred undergo a metamorphosis. They cast their skins two or three times, get rid of their long swimming tails, acquire a cylindrical shape and, ultimately, along with increased size, develop a tripartite arrangement of the extreme posterior end, which recalls a similar arrangement

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in the tail of *F. bancrofti* and of *F. recondita* towards the termination of the stay of the former nematode in the mosquito, and of the latter in the dog-flea (Grassi).

Mode of infection.—The metamorphosis of *D. medinensis* in cyclops was discovered by Fedschenko in Turkestan. His observations I have been able to confirm in England; but, owing to the colder climate of the latter country, in English cyclops the

Fig. 110.—Embryos of D. medinensis in body-cavity of cyclops. The cyclops has been slightly compressed so as to force out some of the worms, which can be seen escaping from ruptures at the head and tail. (*From a photograph by Mr. Andrew Pringle.*)

metamorphosis takes somewhat longer to complete; eight or nine weeks, instead of five weeks, as in Turkestan. Fedschenko supposed that the cyclops containing the larvæ of the guinea-worm, on being swallowed by man in drinking water, was digested; and that the parasite, being then set free, worked its way into the tissues of its new and definitive host; but all the experiments he made to bring about infection by means of

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ingestion of cyclops containing dracunculus larvæ gave a negative result. These failures led to the belief that the larvæ might have to undergo further changes before it was fitted for life in man. Considering the peculiar geographical limitations of this helminthiasis, and the very general distribution of cyclops, such an arrangement seemed likely enough.*

Quite recently, Leiper has shown that when an infected cyclops is transferred to a 0·2 per cent. solution of hydrochloric acid it is immediately killed, but the larvæ, so far from being destroyed, are aroused to great activity, and eventually escape into the fluid, in which they swim freely. From this he conjectured that under natural conditions man becomes infected through the ingestion of infected cyclops, the gastric juice acting on cyclops and larva in the same way as the hydrochloric acid in his experiment. In order to prove this he fed a monkey on bananas concealing cyclops which had been infected for five weeks, and which contained fully developed larvæ. Six months later, when the monkey died, five worms were found in its connective tissues, all possessing the anatomical characteristics of *D. medinensis*.

The evidence is now fairly complete that the life-span of the female dracunculus extends to about one year, conforming probably to the habits of certain species of cyclops which, under natural conditions, serve as its intermediary host. It is not to be supposed that every species of cyclops is an effective intermediary; for, were this the case, guinea-worm would have a much wider geographical range.

Biological peculiarities explained.—The little we now know of the life-history of the guinea-worm explains many things that were formerly mysterious. We now understand why the parasite, on attaining maturity, makes for the legs and feet; these are the parts of the human body most likely, in tropical

* One German observer has stated that he succeeded in communicating guinea-worm to a monkey by applying living embryos to the skin of the animal.

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countries, to come in contact with puddles of water, the medium in which cyclops—the intermediary host —lives. We can understand, also, why it is that the contact of water with the skin of the host causes the guinea-worm to expel her young; and we can understand the rationale of the douching, so much practised by the natives of certain of the endemic districts, in their attempts at extraction. The water-carriers in India are said to be very subject to guinea-worm, which, in their case, is prone to appear on the back—that is, the part of the body against which the water-skin lies when being carried. On this fact has been based an hypothesis that the young guinea-worm enters by the skin. I would interpret the fact, if fact it be, by suggesting that the mature guinea-worm, conformably to her instinct, seeks out that part of the body most in contact with water, which, in the case of the Indian water-carrier, is his back.

Premature death of parasite.—Occasionally the guinea-worm fails to pierce the integument of her host; sometimes she dies before arriving at maturity. In either case she may give rise to abscess; or she may become cretified and in this condition may be felt, years afterwards, as a hard convoluted cord under the skin of the leg, or be discovered only on dissection.

Treatment.—Formerly it was the custom, so soon as a guinea-worm showed itself, to attach the protruding part to a piece of wood and endeavour to wind her out by making a turn or two of this daily. Sometimes these attempts succeeded; just as often, the worm snapped under the strain. The consequences of this accident were often disastrous. Myriads of young escaped from the ruptured ends into the tissues, and violent inflammation and fever, followed by abscess and sloughing, ensued; weeks, or months, perhaps, elapsed before the unhappy victims of this rough surgery were able to get about. Too often serious contractions and ankyloses from loss of tissue and inflammation, and even death from septic trouble, resulted.

If a guinea-worm be protected from injury, and

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the part she occupies frequently douched with water, her uterus will be gradually and naturally forced out inch by inch and emptied of embryos. Until this process is completed she resists extraction; possibly the hook at the end of her tail assists her to maintain her hold. When parturition, in from fifteen to twenty days, is completed, the worm is absorbed or tends to emerge spontaneously. A little traction, if practised then, may aid extrusion. Traction, however, must not be employed so long as the embryos are being emitted. The completion of parturition can be easily ascertained by the douching experiment already described.

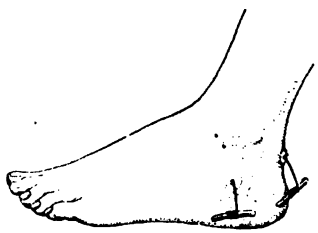

Fig. 111.—Filaria medinensis being extracted from foot.

Emily, a French naval surgeon, has introduced a system of managing guinea-worm cases which bids fair to shorten treatment and obviate the serious risks of the old winding-out system. By means of a Pravaz's syringe he injects the body of the worm, if she chances to be protruding, with solution of bichloride of mercury, 1 in 1,000. This kills the parasite; after twenty-four hours, extraction is generally easily effected. If the worm has not shown herself externally, but can be felt coiled up under the skin, he injects as near the coils as possible, and through several punctures, a few drops of the same solution. This, too, kills the parasite. Her body is then absorbed, as a piece of aseptic catgut would be, without inflammation or reaction of any description; or she may be cut down on, and easily extracted. Others have confirmed the value of Emily's method, which saves much time and suffering and, with due care, is devoid of risk.

Prophylaxis.—From what has been stated with regard to the *rôle* of cyclops, it is evident that the prevention of guinea-worm is merely a question

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of protection of drinking water from pollution by the subjects of guinea-worm infection.

FILARIA LOA.

Synonyms. — *Dracunculus oculi* — *D. loa* — *Filaria oculi*—*F. subconjunctivalis*—*F. diurna and F. bourgi.*

History.—*Filaria loa* has been known for over three hundred years. Although undoubtedly of African origin, the earlier described cases were in negroes in the West Indies who must have acquired their parasites in West Africa prior to their deportation as slaves to America. For long the worm was regarded as an immature dracunculus. Since the characters of the parasite have been more carefully studied this view can no longer be held, and *F. loa* is now thoroughly established as a distinct species.

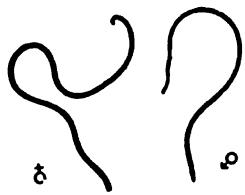

Fig. 112.– Filaria loa (nat. size).

In 1891 I found in the blood of two negroes—one from the lower Congo, the other from Old Calabar—certain microfilariæ morphologically closely resembling that of *F. bancrofti*, but differing from the latter, inasmuch as they came into the peripheral circulation during the day and disappeared from it during the night. As in one of these negroes *F. lóa* had formerly been seen in his eye, I suggested that the new microfilaria, which I named *F. diurna*, was the hæmatozoal larval form of *F. loa*. This view was supported by the fact that in fragments of a loa which I received from Leuckart the contained embryos appeared to be identical in every respect with *F. diurna*. Nevertheless, I failed in several cases of *F. loa* infection to find *mf. diurna* in the blood.

In 1901, Dutton, Annett and Elliot had the opportunity of studying *F. diurna* in its own habitat in West Africa, and came to the conclusion that my hypothesis as regards the relationship of *mf. diurna*

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and *F. loa* was erroneous, contending that *mf. diurna* was none other than *mf. bancrofti*, whose normal periodicity had been disturbed by the peculiar habits of those West African negroes who, they tell us, spent their nights in orgies.

Sambon, refuting the theory of the Liverpool Commission, again pointed out the similarity of *mf. diurna* to the larvæ still contained within the uterus of *F. loa*, and explained that the lack of contemporaneousness between *mf. diurna* and *F. loa* in the same patient is probably due to the fact that this long-lived parasite does not produce its young until after a long period of wanderings when, having attained full maturity, it retires into deeper structures for parturition. He pointed out that the majority of filariæ removed whilst wandering beneath the skin of patients were more or less immature forms; that in young children *F. loa* is as a rule the only form found, whilst in adults *mf. diurna* is the commonest finding, with frequently the history of a previous loa, and finally that *F. equina* of horses and asses, also found in or about the eyes of the host in its immature or barely mature stages, descends into the peritoneal cavity for parturition when fully mature.

Later, an association was discovered between *F. loa* and the disease known as Calabar swellings, and, also, between Calabar swellings and *mf. diurna*. Moreover, as a considerable number of cases of *F. loa* concurring with *mf. diurna* have now been recorded by Prout, Henley, Brumpt, Wurtz, Penel, Kerr and myself, and as the concurrence of the geographical range of the two forms of parasitic infection has been fairly well made out, there can be little doubt that *F. loa* and *mf. diurna* are respectively the mature and larval form of the same species.

Geographical distribution.—We have no definite knowledge of the extent and details of the geographical range of *F. loa*. It appears to be widely distributed throughout tropical West Africa from Sierra Leone to Benguella. In some parts—as in Old Calabar, Cameroons, and the Ogowé River—a

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very large proportion of the inhabitants are affected. How far it penetrates into the interior of the Continent is as yet unknown. I have seen several cases in Europeans from the Upper Congo within a few miles of the Stanley Falls. Brumpt records its presence in Kassai, approximately 600 miles from the coast on one of the chief tributaries of the Congo. The larval form (*mf. loa*) has been found twice by Cook in Uganda; but such isolated findings cannot be taken as landmarks, seeing that *F. loa* is a long-lived parasite and its hosts may have contracted the infection years previously, and at a distance from the place at which it was recognised. At the time of the slave trade numerous cases were reported from the West Indies and South America, but always in negroes from Africa, and their occurrence ceased with the abolition of slavery. The suggestion that about 1795 there existed an endemic centre for this parasite in San Domingo is based on very doubtful evidence. Nowadays, cases are occasionally seen in Europe and America, in both negroes and whites, but only in persons who have frequented those parts of Africa inhabited by the parasite. Possibly, on account of the opening of new trade routes and of the more frequent intercourse between the natives, *F. loa* may greatly extend its range in Africa.

Zoological distribution.—Hitherto *F. loa* has not been seen by reliable observers in animals, but, according to Plehn, the natives of Cameroons assert that it occurs in goats and sheep.

Specific diagnosis.—*F. loa* is especially characterised among the nematodes of man by the presence of numerous, rounded, smooth, translucent protuberances of the cuticle, 12–16μ in diameter and rising 9-11μ above the general surface. These chitinous bosses vary greatly in number and arrangement on different specimens and are, as a rule, more numerous on the female. Their distribution is very irregular. In the male they are wanting at the extremities, beginning about 1·5-2·5 mm. from the mouth and tail-tip respectively. In the female they usually extend to the posterior extremity and may also be found on the cephalic end.

The body is filiform, cylindrical, whitish, semi-transparent. Anteriorly, it tapers somewhat abruptly to the mouth, which is terminal, small, simple, unarmed, and apparently destitute of papillæ. There is no distinctly marked neck, but there is a

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sort of shoulder at about 0·15 mm. from the mouth, and at about this level are two small papillæ, one corresponding to the dorsal, the other to the ventral median line.

The posterior extremity of the female is straight, attenuated and broadly rounded off. That of the male is slightly curved ventrally and provided with two lateral expansions of the cuticle (0·7 mm. long by 0·029 mm. broad), situated nearer the ventral than the dorsal surface. In the middle of the ventral surface, between the lateral alæ, and at about 0·080 mm. from the tail-tip, is the opening of the ano-genital orifice from which two unequal spicules may be seen pro-

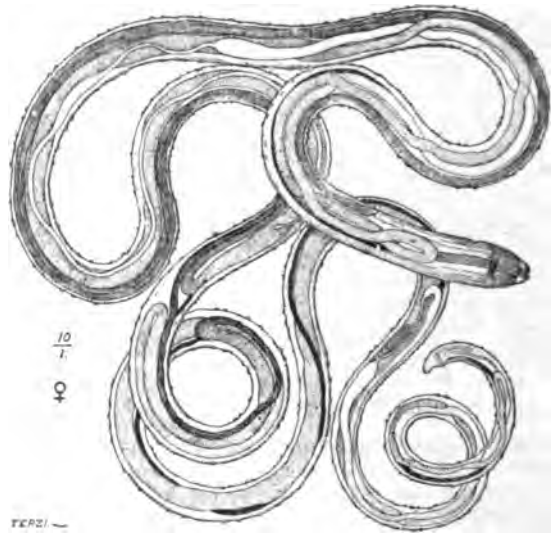

Fig. 113.—F. loa, female. (*Partly after Looss.*)

truding. The opening is surrounded by thick labia. On either side, and somewhat asymmetrically placed, are four large globular and pedunculated papillæ closely approximated and decreasing in size antero-posteriorly. Further back, and nearer to the middle line, is a fifth symmetrical pair of very small conical postanal papillæ with broad base and acuminated point. (Fig. 116.)

The adult male worm measures 30–34 mm. in length, and presents a maximum breadth of 0·350–0·430 mm. in the anterior part of the body. The posterior part tapers gradually towards the tail. The measurements of the adult female have not been satisfactorily determined. The specimens so far

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examined, extracted from under the skin, or from about the eyes of patients, varied greatly in length*—20 mm. (Blanchard); 27 mm. (Leuckart); 32·3 mm. (Manson); 50 mm. (Annett, Dutton and Elliot); 52 mm. (Looss); 55 mm. (Ozzard); 60 mm. (Brumpt); 70 mm. (Maurel).

The alimentary tube begins at the oral cavity, which is funnel-shaped and surrounded by a strong muscular mass. It consists of a slender œsophagus without bulb, of an intestine attaining a width of about 65 μ towards the middle of the body, and of a short, attenuated rectum.

The male reproductive organ is first encountered at about 3 mm. from the cephalic extremity, where it ends in a pointed

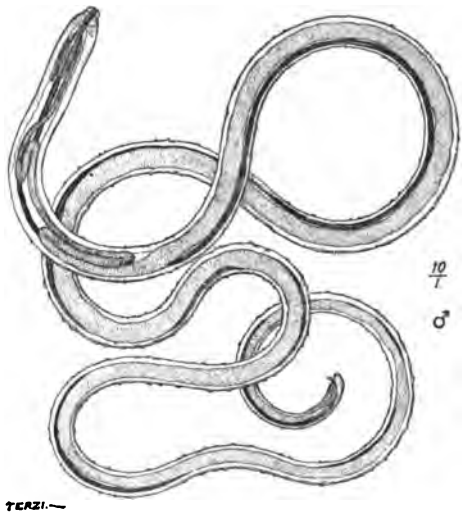

Fig. 114.—F. loa, male. (*Partly after Looss.*)

blind sac. Anteriorly, it is very sinuous and winds round the alimentary canal; posteriorly it straightens, attains a diameter of 85–105 μ, and terminates by a vesicula seminalis filled with more or less spherical spermatozoa 6—8 μ in diameter.

In the female the vulva forms a small eminence at about 2·5 mm. from the anterior extremity. The vagina, 9 mm. long and 95 μ wide, branches off into two long tubes extending almost throughout the entire length of the body. These tubes,

* If the record of Guyon (1864) that his specimen was 15 cm. long does not rest on an error in transcribing or printing, it shows that the fully grown female is really much larger than we know at present from the extracted subcutaneous specimens.

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the narrow ends of which are the ovaria, contain eggs in all stages of development as well as free larvæ 0·253–0·262 mm. in length by 0·0047–0·005 mm. in breadth.

Structure of the larval form.—*Microfilaria loa* (= *diurna*) is very similar in size (298 μ by 7·5 μ) and structure to *microfilaria bancrofti*. Like the latter, it is enclosed within a "sheath," its tail is pointed, and it has the same V and tail spots.

Their respective periodicities are very characteristic; more so, apparently, in the case of *mf. loa* than in that of *mf. bancrofti*; for, whereas by inverting the sleeping habits of a subject of *F. bancrofti* infection it is easy to invert or disturb the periodicity of the microfilariæ, this cannot be done in the case of *mf. loa*. Unfortunately, I can adduce only one experiment in support of this remarkable circumstance; but that experiment was a very thorough and carefully conducted one, and extended over a

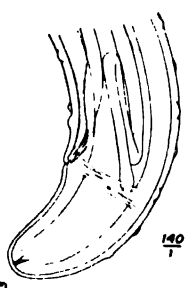

Fig. 115.—Posterior extremity of F. loa, female. (*After Looss.*)

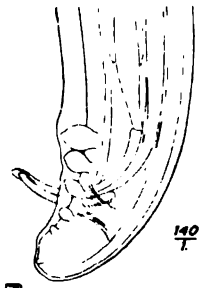

Fig. 116.—Posterior extremity of F. loa, male. (*After Looss.*)

considerable period. During all the time the patient (who had had several *F. loa* excised at different times and who was still showing signs of their presence) slept during the day and kept awake during the night; nevertheless, the microfilariæ continued to appear in vast numbers in the peripheral blood during the day, but were only very rarely found in it during the night.

Although in the fresh liquid blood it is practically impossible to distinguish, with the microscope alone, the living *mf. loa* from the living *mf. bancrofti*, in dried and stained films certain more or less pronounced differences can be made out. (1) In such preparation *mf. bancrofti* is usually disposed in sweeping and graceful curves, such as a skilled penman might make (Plate v., Fig. 1); *mf. loa*, on the other hand, assumes a stiff, ungraceful almost angular attitude like the flourishes made by a schoolboy (Plate v., Fig. 3). (2) The tail end of *mf. loa* is often disposed in a series of sharp flexures, giving it in some instances a corkscrew-like appearance, the extreme

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tip being always sharply flexed. (Plate vi.) (3) The nuclei of the central column of cells of *mf. loa* are larger and stain less deeply than those of *mf. bancrofti*, and, as a rule, the cephalic end of the column is more abruptly terminated in the former. Although in most slides one or two specimens may be hard to diagnose, on the average of a series of preparations the foregoing distinctions are recognisable.

Life history.—Of the life history of *F. loa* little is positively known. As the larval form comes into the peripheral circulation of the human host, it is very probable that, like *mf. bancrofti*, it is liberated by some blood-sucking insect; and, seeing that it approaches the surface of the body only during the daytime, this must be a blood-sucker of diurnal habit.

Several years ago I called attention to the so-called "mangrove flies" as possible intermediaries; but, so far, very little has been done to elucidate the interesting and important question of the transmission of *F. loa*. Annett, Dutton and Elliot found that *Anopheles* (= *Pyretophorus*) *costalis* served in West Africa as an intermediary host for *F. bancrofti*, but not for *F. loa*, and they suggested, against their own theory of identity, that the latter might be transmitted by some mosquito of diurnal habits. The species most likely to bite during the daytime is *Stegomyia fasciata*. This gnat occurs in West Africa and is said to be capable of fostering *F. bancrofti*; but the abundance of *Stegomyia fasciata* and the absence of *F. loa* in the West Indies and on the adjacent coast of South America, notwithstanding that the latter was often imported there at the time of the slave trade, is opposed to this suggestion. Brumpt examined a number of *Culicinæ*, *Anophelinæ* and *Glossinæ* on the Upper Congo, but never found in any of these developmental stages of *F. loa*. Possibly the appropriate intermediary host is to be found amongst the cleggs, horse-flies or breeze-flies (*Tabanidæ*), large blood-sucking flies with broad head, flat abdomen, and strong legs, which bite during the warmest hours of the day. It is to these insects that the name of "mangrove flies" is usually applied. Numerous species belonging to this family of Diptera, and more particularly to the genera *Tabanus*, *Hæmatopota*, *Pangonia* and *Chrysops*, have a wide distribution in West Africa. Besides the *Tabanidæ*, there are other biting flies belonging to the family *Muscidæ* inhabiting the same localities and, therefore, also called mangrove flies. Amongst these are the tse-tse flies (*Glossinæ*) and the stinging flies (*Stomoxys*). As to the way in which *F. loa* is acquired we have absolutely no information. It would appear that, after it has entered the human body, development is very slow and that probably full maturity is not attained until after several years. In many cases the parasite did not show itself until 3, 4 and 4½ years after the patient had left the endemic area. In one case the parasite was extracted from the eye 13 years after the patient had left Africa; in another the worm or worms appeared at irregular intervals during 15 years.

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Manifestly it is long-lived. An interesting and suggestive evidence of slow development is that, while the immature active worm is often seen in children, the larval form in the blood is found as a rule only in adults. Annett, Dutton and Elliot, in 390 native children of all ages up to about 18 years, examined in a district where *F. loa* was exceedingly common in adults, found *mf. loa* once only in a boy (aged 11).

Slow development and a different habitat at different stages are not peculiar to *F. loa*, only. *F. equina* of the horse and ass and *F. labiato-papillosa* of deer and cattle wander about the subdermal connective tissues and frequently occur in the eyes during their semi-adult stage, but repair to the peritoneal cavity when fully mature. The larvæ of both are found in the blood of the respective hosts, and Noè has shown quite recently that *F. labiato-papillosa* is fostered and transmitted, like *F. bancrofti* and *F. immitis*, by an insect intermediary, to wit, the stinging-fly (*Stomoxys calcitrans*), amongst the cephalic muscles of which it undergoes development.

This slow development of *F. loa* would seem to account for the very frequent failure to find the microfilaria in the blood in cases in which mature parasites have been extracted, which has been brought forward as an argument against the theory that *mf. diurna* was really the offspring of *F. loa*. Some time ago I was consulted by a lady who, for seven years, had been troubled with *F. loa* and Calabar swellings, and had had three loas removed at different times from the neighbourhood of the eye. On examining her day blood I found it full of innumerable specimens of *F. diurna*. That these microfilariæ were *diurna* was fully established by a series of carefully conducted observations carried on day and night for upwards of a week. The patient informed me that she believed the medical man who seven years before had extracted one of the loas from her eye had probably the specimen in his possession still. This I had an opportunity of examining. It was a mature female crowded with embryos in all stages of development, including free larval forms such as were found in the blood. It transpired that I had already, many years before, examined this specimen, and that being interested in the subject I had written for specimens of the day blood of this patient soon after the extraction had been made. On referring to my note-book I found a record of the result of my examination of this blood, and that no microfilariæ were then found. From this it is evident that the mature *F. loa* may be present in the tissues, and yet that embryos may be absent from the blood. I cannot suggest an explanation of what is apparently an anomaly; but the fact is definitely ascertained, and explains how it is that in many of the recorded cases of loa infection the embryos have been absent from the general circulation. It may be that it is not until the gravid female arrives at some organ or tissue that she deposits her young in such a position that they can get access to the circulation, and that the wanderings for which these worms are so remarkable

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are an effort to attain this situation. It would be well for those who have the opportunity, to look for the parasite at autopsies, especially in the serous cavities. Quite recently Penel stated that he had found *mf. loa* in the saliva and urine of a patient who presented this larval filaria in the peripheral circulation.

As yet it is impossible to estimate accurately the number of adult loas present in any given infection, although in advanced cases some idea of this might be got from the number of microfilariæ in the peripheral blood. As a rule, it is safe to conclude that the particular loa that may show itself about the eye or elsewhere is only one of many. Thus, in 1903, Brumpt, at the *post-mortem* of a negro whose blood contained microfilariæ (for which, under the impression that it was a new species, he suggested the name of *F. bourgi*), found in the tissues of the heart five adult worms. Four of these were cretified, but the fifth was alive and contained embryos similar to those in the blood. This worm he subsequently identified as a *F. loa*. In the following year Wurtz found *mf. diurna* in the blood of a Congolese negro suffering from sleeping sickness. On the death of the patient he made a most careful *post-mortem* examination and found two adult loas in the subcutaneous connective tissue of the arm. On the dissection being continued by Penel, over thirty additional specimens, male and female, were discovered under the skin of the limbs. There are not a few instances on record in which two or more loas have been extracted from the same patient. We may, therefore, be practically certain that in nearly every instance of this kind of filariasis the infection is multiple.

Pathogenesis. — As already stated, *F. loa* during the period of its growth and development in man makes frequent excursions through the subdermal connective tissues. It has been noticed very frequently beneath the skin of the fingers, and it has been excised from under the skin of the back, from above the sternum, from the left breast, the lingual frenum, the loose skin of the penis, the eyelids, the conjunctiva, the anterior chamber of the eye. Ziemann says that it may wander about the scalp. The parts most frequently mentioned are the eyes, and, although they may have attracted more attention when in this situation, it seems as if the worm has a decided predilection for the eye and its neighbourhood. A patient informed me that the average rate at which a loa travelled was about an inch in two minutes. Both he and others have told me that warmth, such as in sitting before a fire,

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seemed to attract them to the surface of the body. As a rule, the migrations of the parasite give rise to no serious inconvenience, but they may cause pricklings, itching, creeping sensations and, occasionally, transient œdematous swellings, "Calabar swellings," in different parts of the body. When the parasite appears under the conjunctiva it may cause a considerable amount of irritation and congestion; there may be actual pain even, associated with swelling and inability to use the eye and, perhaps, tumefaction of the eyelids. Should a loa wander into the vicinity of such a situation as the rima glottidis or the urethra the consequences might be serious.

CALABAR SWELLINGS.

Under this name Thompstone describes certain fugitive swellings which are of frequent occurrence in parts of tropical West Africa—Southern Nigeria to Benguella and inland to the Upper Congo. They are found in natives and Europeans alike. I have seen many cases in Englishmen, especially in officials from the neighbourhood of Old Calabar. Thompstone says "the swellings are about the size of half a goose egg, painless, though somewhat hot, both objectively and subjectively, not pitting on pressure, and usually disappear in about three days. They come suddenly and disappear gradually, and occur in any part of the body." Thompstone never saw more than one swelling at a time. They recur at irregular intervals and, it may be, during many years after the patient has returned to Europe. In some instances the swelling seems to be induced by the rubbing provoked by the irritation accompanying the presence of a *F. loa* just under the skin, in other instances they develop spontaneously. When occurring in the hand, or about the forearm, they may give rise to a sensation of powerlessness and soreness as if the part had received a blow. They never suppurate.

Although in a large proportion of cases *F. loa* larvæ cannot be found, in others either the parent worm has shown itself on the eye, or its microfilariæ have been detected in the blood. The latter circum-

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stance, together with the geographical feature of the endemicity of these swellings and their clinical characters, make it practically certain that they are somehow produced by *F. loa*. On the supposition that the swelling might be caused by the emission of her larvæ by a parent loa into the connective tissue, I endeavoured in one case, by aspirating the centre of the swelling with a hypodermic syringe, to substantiate this speculation; the result was negative. The mechanism of their production, therefore, is still an unsolved problem.

FILARIA VOLVULUS, LEUCKART, 1893.

History.—*Filaria volvulus* was discovered by a German medical missionary, who noticed peculiar worms in two tumours, the size of a pigeon's egg, which he had removed, one from the scalp, the other from the chest, of Gold Coast negroes. The tumours were forwarded to Leuckart, who described and named the parasite in 1893. In 1899, Labadie-Lagrave and Deguy found an immature female filaria, which Blanchard identified as *F. volvulus*, in a small tumour removed from the arm of a soldier, who must have contracted the infection six years previously whilst campaigning in Dahomey. Labadie-Lagrave and Deguy were able to show that the parasite occupied a lymphatic vessel. In 1901 Prout described two cases from Sierra Leone. Brumpt, during his travels through Central Africa, had the opportunity of examining numerous cases. Recently Fülleborn and Parsons have added considerably to our knowledge of this parasite.

Geographical distribution. — The earlier cases were reported from the West Coast of Africa —Sierra Leone, Gold Coast, Dahomey. Brumpt met with his cases along the Welle between Dongon and M'Binia. He believes that in that region *F. volvulus* affects about 5 per cent. of the riverine population. He saw cases on the Himbri, and he refers to others on the Kibali and on several of the tributaries of the Welle. Cooke met with cases in Uganda, Fülleborn in Cameroons, Parsons in Northern Nigeria.

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Description of parasite.—According to Parsons, the adult male is 20-32 mm. in length by 0·2 mm. in breadth. The body is white, filiform, tapering at both ends. The head is rounded and has a diameter of 0·04 mm. The cuticle is transversely striated. The mouth is unarmed. The alimentary canal is straight and ends in a subterminal anus. The tail terminates in a single spiral, and is bulbous at the tip. There are two pairs of preanal papillæ, two pairs of postanal papillæ, and an intermediate single large papilla. Two unequal spicules may be seen protruding from the cloaca.

According to Braun, the adult female measures 60-70 mm. in length by 0·36 mm. in breadth. The head is rounded and truncated; it measures 0·04 mm. in diameter. The tail is curved. The striations of the cuticle are not so distinct as in the male.

The larva measures about 300 μ in length; it has no "sheath." The body tapers from about the last fifth of its length and terminates in a sharply pointed tail. At about the anterior fifth of the body there is a gap in the central column of cells (V spot).

Pathogenesis.—*F. volvulus* is found in peculiar subcutaneous tumours, the size of a pea to that of a pigeon's egg. The same patient may present one or several of these tumours. The regions of the body most frequently affected are those in which the peripheral lymphatics converge. Thus they are usually found in the axilla, in the popliteal space, about the elbow, in the sub-occipital region and in the intercostal spaces. The tumours are never adherent to the surrounding structures and can be easily enucleated. They are formed of a dense mass of connective tissue, which enwraps the parasites and encloses small cyst-like spaces filled with a greyish viscous substance consisting almost entirely of microfilariæ. The position of the adult worms within these tumours is very remarkable. The greater length of their coiled-up bodies is embedded in the connective stroma, but the posterior extremity of the male with its copulating organs, and the anterior extremity of the female with its vaginal opening, are free in one of the spaces.

The formation of the tumours is elucidated by Labadie-Lagrave and Deguy's case. The authors found an immature female *F. volvulus* in a lymphatic vessel partly obstructed by an infiltration of fibrin and leucocytes. It appears, therefore, that the presence of the parasites within the lymphatics gives

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rise to an inflammatory process, and that the consequent fibrinous deposit envelops the parasites, obliterates the lumen of the vessel, and ultimately isolates the affected tract. According to the natives, the tumours may last indefinitely, and seldom ulcerate. Some old patients told Brumpt that their tumours had been present since childhood.

Life history.—Nothing is known of the life history of this filaria. Its larvæ have not been found in the peripheral circulation, whether by day or by night. Brumpt, however, from the examination of numerous sections of filarial tumours, is confident that the microfilariæ leave the cysts. He has seen them round the periphery of the tumours and believes they may reach the lymphatics and thence the general circulation. He even suggests that the infection is probably transmitted by some blood-sucking insect, and, considering its riverine distribution, he points more especially to the Glossinæ.

SPARGANUM MANSONI (Cobbold).

Synonyms.—*Ligula mansoni, Bothriocephalus liguloides, B. mansoni, Dibothrium mansoni.*

This parasite, the larva of a cestode belonging to the family Dibothriocephalidæ, and, provisionally, to the artificial collective group Sparganum,* was discovered in 1882 by the writer in making the *post-mortem* examination of a Chinese in Amoy. So far only the larval form is known, the size varying according to stage of development. The following measurements have been given: Length, 8 to 36 cm.; breadth, 0·1 to 12 mm.; thickness, 0·5 to 1·75 mm. My own specimens measured about 30 to 35 cm. in length, by about 2·5 mm. in breadth. During life they are extremely elastic, after immersion in alcohol they contract and wrinkle. The anterior end is broader than the posterior, is rounded, and presents a papilliform projection on which is found the compressed and more or less completely invaginated head. The

* This group includes larval stages of bothriocephaloid worms which have not reached a stage in development enabling determination of genus.

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body is flat, unsegmented and transversely wrinkled. On the ventral surface there is as a rule a distinct longitudinal median groove; on the dorsal surface there may be two longitudinal grooves. No sexual organs are present.

In my case the parasites (11) lay under the peritoneum in the neighbourhood of the kidneys and iliac fossae, and (1) apparently free in the pleural cavity. They were more or less coiled up and irregularly disposed in the subperitoneal fascia, looking like ribbon-strings of fat until turned out, when

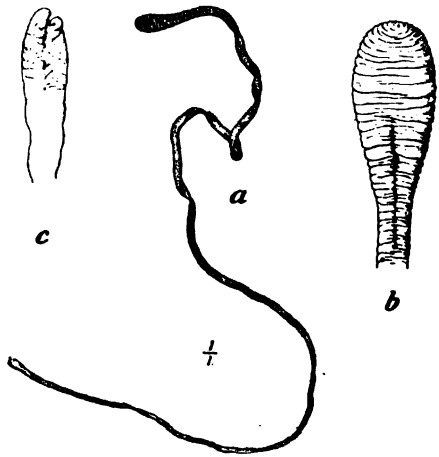

Fig. 117.—Sparganum.
a, Natural size; *b*, anterior extremity; *c*, posterior extremity, extracted from an abscess in a Masai. (*After Sambon.*)

they exhibited feeble yet distinct movements. Scheube found a specimen in the urethra of a Japanese. Ijima and Murata also found the same parasite in the urethra, the worm appearing during micturition with its head projecting from the urethra and occluding it. Thrice very young specimens have been found in Japan lying beneath the conjunctiva and producing swellings the size of a bean. In one of the Japanese cases the parasite was found in the subcutaneous connective

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tissue of the thigh, where during nine years it gave rise to indolent tumours that recurred fairly regularly every summer at about the same spot; it seemed to change its position very readily, disappearing in about ten days. At the time of its last appearance the swelling attained the size of a fist; an abscess formed from which the worm was extracted. A similar parasite, identified by Sambon, was likewise extracted from an abscess on the thigh of a Masai, in German East Africa, by Baxter; and another was found by Daniels in a Carib in British Guiana.

Nothing is known of the life history of this worm. Leuckart conjectures that the definitive host is probably a carnivorous animal closely associated with man, possibly the dog, the cat, or perhaps the pig. Looss believes that it is an aquatic animal (a bird or a fish) because the parasite appears to endeavour to leave the body of its intermediary host. Analogy and structure suggest that on entering the definitive host the body of the parasite disappears and a tapeworm strobila develops from the posterior part of the surviving head and neck, as in *Cysticercus fasciolaris* of the mouse, or in the plerocercoid of *Dibothriocephalus latus*.

SPARGANUM PROLIFERUM (Ijima, 1905).

Synonyms.—*Plerocercoides prolifer*, *Plerocercus prolifer*.

History.—*Sparganum proliferum* has been reported but once, from Tokyo, Japan. It was found encysted in the subcutaneous tissue in man.

According to Ijima, who describes it, this larva may attain 1–12 mm. in length by 2·5 mm. in breadth. The anterior extremity is narrower and more motile than the posterior end, and may exhibit an apical depression which possibly serves as a sucker. The body, with the exception of the head, contains a number of roundish calcareous corpuscles, and in older specimens there are also reserve-food bodies irregularly distributed. These larvæ can multiply by transverse fission. They give rise to supernumerary heads, which become independent. There are no genital organs.

In the single case reported thousands of parasites were present. In a small piece of skin, 11 cm^2, Ijima found as many as 60. The worms occupied small roundish or ovoid cysts (1 to 8 mm. long by 2 to 5 mm. in width) in the sub-

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cutaneous cellular tissue. The cysts could be enucleated quite easily, and contained one or more parasites. They had been present for over two years, causing an enlarged condition of the thigh and an acne-like appearance of the skin. The patient was 33 years old, and, eight years previously, had suffered from intestinal tæniasis.

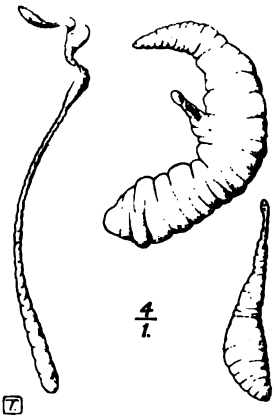

Fig. 118.—Different forms of Sparganum proliferum. (*After Ijima.*)

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CHAPTER XLIII

III. PARASITES OF THE LUNGS

ENDEMIC HÆMOPTYSIS

PARAGONIMUS WESTERMANI (Kerbert, 1878)

Synonyms.—*Distoma westermani, D. ringeri, D. pulmonis, D. pulmonale, D. cerebrale, Mesogonimus westermani, M. pulmonalis, M. ringeri.*

Geographical distribution.—Endemic hæmoptysis occurs in China, Japan, Corea, Formosa, and the Philippines. In many of the endemic districts a notable percentage of the population is affected. It is not improbable that, as knowledge extends, the disease will be found to exist in other countries. Recently the parasite which gives rise to this peculiar form of blood-spitting has been found in the United States in the cat, in the dog, and in the domesticated hog; ere long, therefore, we may hear of endemic hæmoptysis in America. The Chinese and Japanese are nowadays to be found in almost every land, and doubtless they carry with them their peculiar parasites—*Opistorchis sinensis, Fasciolopsis buskii,* and also *P. westermani.*

Symptoms.—The subjects of endemic hæmoptysis have a chronic cough, which is usually most urgent in the morning on rising. The fits of coughing eventuate in the expulsion of a peculiar rusty brown, pneumonic-like sputum. This sputum can be produced at will almost at any time, and often in considerable quantity. In addition to the chronic cough and the tenacious rusty expectoration referred to, the patient is liable to irregular attacks of hæmoptysis. Though usually induced by violent exertion, occasionally such attacks come on without apparent cause. The hæmoptysis may be trifling; on the other hand, it may be so profuse as to threaten life—at all events, to cause intense anæmia.

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The sputum.—On placing a minute portion of the viscid, pneumonic-like sputum under the microscope, its peculiar colour is found to be due partly to red blood corpuscles, partly to a crowd of dark brown, thick-shelled, operculated ova (Fig. 119). These ova vary a good deal in size and shape; they are all distinctly oval, have a yellow, smooth, double-outlined shell, and measure from 80 to 100 μ in length by 40 to 60 μ in breadth. If the sputum be shaken up

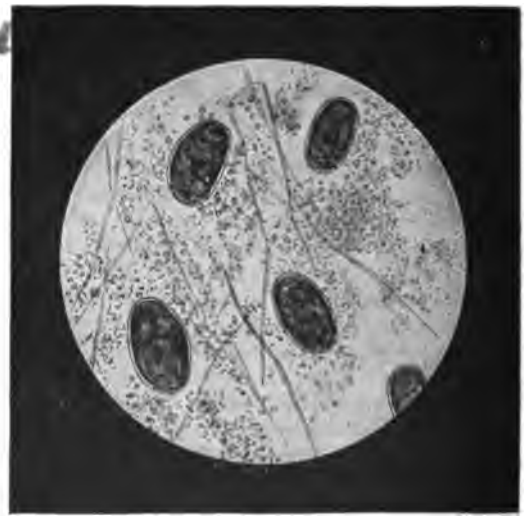

Fig. 119.—Ova of Paragonimus westermani in sputum.

in water, and the water be renewed from time to time, in the course of a month or six weeks—longer or shorter according to temperature—a ciliated embryo (miracidium) is developed in each ovum. When the ovum is mature, on placing it on a slide and exercising slight pressure on the cover-glass, the operculum will be forced back, and the miracidium will immediately emerge and at once begin to swim and gyrate in the water. Farther than this the life-history of the larva has not been traced; but,

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doubtless, it is continued in some fresh-water animal, through which it finds its way back, in a more or less direct way, to man.

Pathological anatomy.—On making a section of the lungs in this disease, a larger or smaller number of what are known as "burrows" are discovered scattered about this organ, particularly towards the periphery. These burrows consist of areas, some-

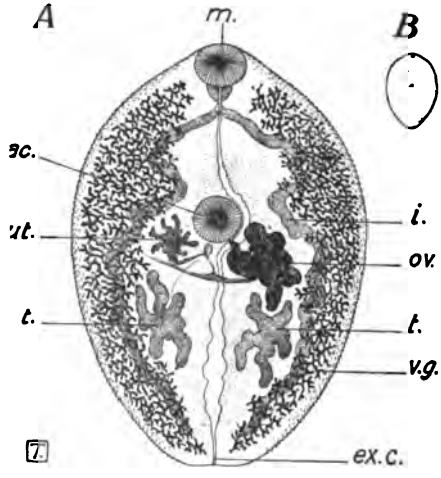

Fig. 120.—Paragonimus westermani. (*Partly after Looss.*)
a, Magnified; *b*, natural size.

what larger than a filbert, of infiltrated lung tissue in which can be seen a number of tunnels filled with the same material that constitutes the characteristic sputum, and also containing one, two, or more small trematodes. The septa between the tunnels may break down and a considerable cavity be thus produced; and as this occurs in connection with one of the bronchi, with which the tunnels always communicate, it may give rise to the appearance of a dilated bronchus. One burrow may communicate with another.

When first discovered it was supposed that *P.*

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westermani was confined to the lungs. We now know that it may affect the liver, peritoneum, testes, intestine, skin, muscle, and brain. In the brain it forms a sort of tunnelled tumour similar to those in the lungs, and by the pressure or irritation proceeding from this tumour may give rise to a peculiar and ultimately fatal form of Jacksonian epilepsy.

The parasite.—The parasite itself is reddish brown in colour, thick and fleshy, and oval in form. So thick is it that its transverse section is almost round. It measures 8 to 16 mm. in length by 4 to 8 mm. in breadth, and is covered with broad scale-like spines. The anterior extremity is bluntly rounded and without cephalic cone; the oral sucker (0·88–1·12 by 0·80–0·83 mm.) terminal or sub-terminal; ventral sucker (0·88–1·2 by 0·86–1·44mm.) slightly larger than the oral sucker and situated somewhat anteriorly to the middle of the body. The pharynx is elongate, but the œsophagus is very short, so that the bifurcation of the intestine is considerably anterior to the ventral sucker. The intestinal cæca run somewhat zigzag to the caudal end of the body. The genital pore opens close to the posterior margin of the ventral sucker. The testes are tubular, ramified, and situated on each side of the middle line, one slightly posterior to the other. The ovary is branched and is placed somewhat posterior to the ventral sucker, and either to the right or left of the middle line. The shell gland is lobate; the uterus short and usually massed; the vitellaria are marginal and greatly developed.

Diagnosis.—Diagnosis of endemic hæmoptysis is at once established by the discovery of the characteristic ova in the almost equally characteristic sputum. Râles and other physical signs of lung consolidation are not usually discoverable.

In the case of one-sided convulsions, or in hemiplegic affections occurring in a native of or in a visitor from the countries in which this trematode is endemic, the sputum should be examined on the chance of discovering evidence of the parasite. Should ova be found, there is a strong presumption that the cerebral trouble arises from trematode tumour in the brain.

Treatment.—Hitherto no means of expelling this parasite from the lungs has been discovered. In the case of cerebral distomatosis it might be possible by an operation to remove the parasite and associated

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tumour, and thus afford a chance of recovery in what has hitherto proved a fatal condition.

Prophylaxis in this, as in so many animal parasitic diseases, principally lies in the direction of securing a pure water-supply and avoiding all uncooked articles of diet which might be supposed to contain the young parasites. The sputum should be destroyed.

NOTE.—Musgrave (*Philippine Journal of Science*, March, 1907) has recently shown that paragonomiasis is not uncommon in the Philippines. He met with seventeen cases in one year. He gives a detailed account of the pathological anatomy of this helminthiasis, bringing out especially the important fact that in a proportion of instances the infection is of a general character, the peculiar bluish cyst-like burrows of the parasite occurring in many organs and tissues. The infiltration of the tissues by the eggs produces, especially in serous membranes, little brownish-red patches, sometimes quite visible to the naked eye. The intestinal submucosa is a common seat of infiltration, and here the presence of the ova may give rise to inflammatory reaction, ending, perhaps, in ulceration and in the appearance of ova in the stools.

In reading Musgrave's paper I was particularly struck by the statement that in one of his cases he found no fewer than 100 mature parasites congregated in a psoas abscess. It is usually believed that the flukes enter their vertebrate hosts as cercariæ, and that they at once proceed to their permanent habitat and to sexual maturity. If this be the case with *P. westermanni*, it is difficult to understand how, without any special anatomical lead, so large a number as 100 cercariæ contrived to arrive at exactly the same spot. It seems to me that this local accumulation of adults could be best explained on the supposition that the infection of the patient took place at some earlier period in the development of the parasite, either in the miracidium, or in the redia stage.

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CHAPTER XLIV

IV. PARASITES OF THE LIVER

OPISTORCHIS NOVERCA; CLONORCHIS SINENSIS; POROCEPHALUS ARMILLATUS

OPISTORCHIS NOVERCA, Braun, 1903

Synonym.—*Distoma conjunctum.*

History.—*Opistorchis noverca* was discovered by MacConnell at Calcutta in 1876. Lewis and Cunningham, who a few years previously had found a similar parasite in the liver of pariah dogs from the same locality, suggested that both their own species and MacConnell's were identical with the *D. conjunctum* (now called *Metorchis conjunctus*) found by Cobbold in the liver of an American fox (*Canis fulvus*) that died in London. In 1903, Braun showed that the Indian trematode belongs to a different species, and gave it the name of *Opistorchis noverca.*

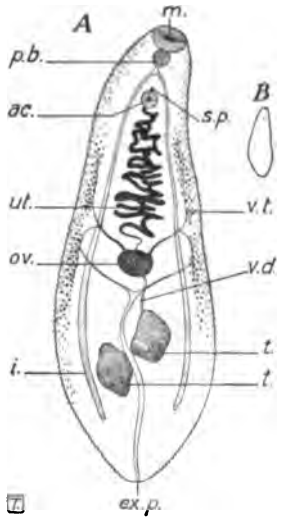

Fig. 121.—Opistorchis noverca. *a*, greatly magnified; *b*, natural size.

Geographical distribution.—India.

Zoological distribution.—As stated above, it has been found in the gall-ducts of the dog (*C. familiaris*).

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Specific diagnosis.—The description of the parasite is chiefly from the data and drawings furnished by MacConnell and needs revision. *O. noverca* is of a lanceolate shape, and more attenuated anteriorly than posteriorly. It measures from 9 to 12mm. in length by 2·5mm. in breadth. The oral sucker is terminal and larger than the acetabulum or ventral sucker, which is situated close to it, just below the bifurcation of the intestine. The cuticle is densely covered with spines. The pharynx is large and globular; the intestinal cæca extend to about the posterior eighth of the body. The testes are in the posterior third and somewhat apart. The anterior one is roundish, the posterior one lobate. The ovary is placed at about the middle of the body. The uterus appears to be poorly developed, its convolutions spreading laterally barely beyond the cæca. The vitellaria appear to extend from acetabulum to posterior testicle. The eggs are oval and measure 34 μ by 19 to 21 μ.

Pathogenesis.—Only two cases have been reported from man, both by MacConnell (1876 and 1878). The parasites were found in large numbers in the bile ducts, which were thickened and sacculated.

CLONORCHIS SINENSIS (Cobbold, 1875).

Synonyms.—*Distoma sinense, D. spathulatum, D. japonicum, D. innocuum, Opistorchis sinensis, Clonorchis endemicus.*

History.—*Clonorchis sinensis* was discovered almost simultaneously by MacConnell in India and MacGregor in Mauritius, in 1874.

Geographical distribution.—It has been found in many Eastern countries, including India, Mauritius, Japan, Korea, Formosa, China and Tonkin. In the last-named country it appears to be very common. In Central Japan, according to Katsurada, there are certain districts in which it affects from 56 to 67 per cent. of the population.

Specific diagnosis.—*C. sinensis* (Fig. 132) measures from 10 to 20 mm. in length, by 2 to 5 mm. in breadth; it is oblong, narrow, flat and somewhat pointed anteriorly, reddish in colour, and nearly transparent. The oral sucker is larger than the ventral acetabulum, which is situated almost on the border between the first and second fourths of the body. The cuticle has no spines. The pharynx is globular and short, the œsophagus is slender and 0·17 mm. long. The bifurcation of the intestine is nearer to the oral than to the ventral sucker. The intestinal cæca are simple, slender, and extend almost to the posterior end of the body. The genital pore opens on the

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middle line immediately in front of the acetabulum. The testes are branched and situated in the posterior portion of the body, one posterior to the other. The ovary is trilobate and anterior to the testes. The uterus is moderately developed, and its coils are anterior to the genital glands. The vitellaria are moderately developed and occupy about the middle third of the body. The eggs are 28 to 30 μ in length by 15 to 17 μ in breadth, operculated, almost black in colour, and contain a ciliated embryo. Nothing is known of the life history of the parasite farther than that it may occur in some of the lower animals—in the cat, for example. Probably its immature stages are passed in a mollusc or other small, soft-skinned, fresh-water animal.

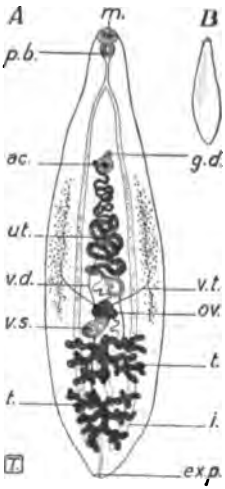

Fig. 122.—Clonorchis sinensis. (*Partly after Looss.*) *a*, Magnified; *b*, natural size.

C. sinensis inhabits the bile ducts and gall-bladder. It dilates and thickens the biliary canals, expanding them in places into cavities and diverticula as large as a filbert. In these cavities vast numbers of parasites are sometimes found. The diverticula communicate with the bile-ducts, along which the ova of the parasites, and sometimes the parasites themselves, escape into the intestine. The affected liver is enlarged as a whole, although the tissue in the immediate neighbourhood of the diseased bile-ducts is atrophied. The spleen, also, may be hypertrophied, and the intestine in a condition of chronic catarrh. Some instances are recorded of the presence of this trematode in the pancreatic ducts, in the duodenum, and in the stomach.

This parasite, which for long was supposed to be practically innocuous, is now held to be the cause of a serious disease of the liver, which may terminate fatally; indeed there can be no doubt of this when one considers that in some of the cases recorded

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several thousand parasites were present. However, we should not forget possible confusion with another grave distomatosis of Japan and other Eastern countries due to *Schistosoma japonicum*.

When the infection is severe the liver becomes enlarged, and chronic diarrhœa, with recurring attacks of jaundice, sets in. Later, anasarca appears and gradually a cachexia, resembling that of sheep-rot, is established, which, in the course of several years, may prove fatal.

It would be well to bear this parasite in mind in approaching the diagnosis of obscure hepatic disease, associated with diarrhœa and jaundice, in patients from the East. It is just possible that the discovery of the ova in the stools might guide to a correct diagnosis.

Treatment.—So far no specific treatment has been found for this disease. The patient should be removed to a non-infected area and given nourishing food. Recently salol has been reported as beneficial in the analogous liver-fluke disease of sheep.

POROCEPHALUS ARMILLATUS (Wyman, 1848).

Synonyms.—*Linguatula armillata, L. constricta, Pentastomum constrictum, P. polyzonum, P. diesingi, P. euryzonum, Nematoideum hominis.*

History.—The larval form of this vermiform arthropod, belonging to the family *Linguatulidæ*, genus *Porocephalus*, was discovered in 1847 by Pruner, who found it, in Cairo, in the liver of two negroes. It must have been found in man before that date, since Pruner himself informs us that he saw two specimens in the Pathological Museum of Bologna labelled "Insects from the liver of man." Subsequently it was found in man by Bilharz, Fenger, Kearney, Crawford, Marchoux, Chalmers and others. In 1852, Von Siebold proposed to call it *Pentastomum constrictum*; but Shipley, in his revision of the family *Linguatulidæ* (1898), points out that the adult form was discovered and named *Linguatula armillata* in 1848 by Wyman, who found it in the lungs of an African python. Shipley further considers that Hoyle's *Pentastomum protelis* from the Aard-wolf (*Proteles cristata*), Wedl's *P. leonis* from the lion, Van Beneden's *P. diesingi* from the mandrill (*Cynocephalus mormon*), and Hartley's *P. polyzonum* from an African python, belong to the same species. He also states that, in accordance with the rules of zoological nomenclature, the generic name

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for the cylindrical *Linguatulidæ* should be *Porocephalus*, a term introduced by Humboldt eight years before Rudolphi proposed the name *Pentastomum*. Neumann (1899) refers the larval forms found in man to *Porocephalus moniliformis*, a species discovered by Diesing in 1836 in the Indian python (*Python molurus*). Looss (1905) is of opinion that Wyman's and Diesing's species are identical. Sambon agrees with Shipley's determination, based principally on the number of rings, which are never more than 22 in *P. armillatus*, but 28 to 30 in *P. moniliformis*.

Geographical distribution.—*P. armillatus* seems to be confined to tropical Africa and hitherto, as regards man, to negroes only. Quite recently Dr. Salm has found a porocephalus encysted beneath the serous coat of the small intestine of a Djambi native in Java. He gives no description but mentions it under the name Porocephalus moniliformus, together with other similar parasites found in the Indian civet and in the tiger.

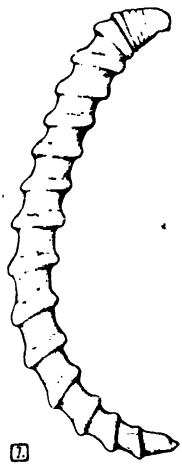

Fig. 123.—Porocephalus constrictum, natural size. (*After Sambon.*)

Zoological distribution.—The adult form inhabits pythons and other snakes. It has been found in *Python sebæ* by Wyman, Sambon and others; in the Royal python, *Python regius*, and in the nose-horned viper (*Bitis nasicornis*) by Sambon. The larval —or, more correctly, the nymphal —form has been found in the lion, in the leopard, in the mandrill, in the Aard-wolf. Pruner found it in the giraffe, Looss in Syke's monkey (*Cercopithecus albigularis*), and Sambon in the Pousargues guenon (*Cercopithecus pousarguei*), and in the African hedgehog (*Erinaceus æthiopicus*).

Description of parasite. — Body vermiform, yellowish translucent, larger in females—9-12 cm. long by 5-9 mm. broad—than in males—3-4·5 cm. long by 3-4 mm. broad. Cylindrical in the anterior half, slightly tapering posteriorly, and terminating in a blunt-pointed cone. It is characterised by the presence of prominent opaque rings 1-2 mm. wide, numbering 16 or 17 in the males, 18 to 22 in the females, placed somewhat obliquely and separated by interannular spaces 2-5 mm. wide except between the first rings, which are faintly indicated by shallow linear furrows. There is no clear distinction between cephalothorax and abdomen, and the rings nearest the cephalothorax are sometimes so

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indistinct that it is almost impossible to make out their actual number. The cephalothorax is depressed, slightly convex on the dorsal surface, more or less concave on the ventral surface. It is rounded anteriorly; posteriorly it is limited by the first body rings. It varies considerably in length; its breadth is from 4 to 7 mm. The mouth, opening on its ventral surface about 1 mm. from the anterior border, is lipped by a chitinous ring. Above it are two prominent papillæ. On either side of the mouth are two protractile chitinous hooks similar in shape to feline claws. The anus is terminal at the posterior end. The genital orifice of the male is at the anterior end of the abdomen in the middle of the ventral surface of the first body ring; that of the female opens in the middle of the ventral surface of the caudal cone at about 1 mm. from the anus. The female is oviparous; the eggs are broadly elliptical.

The nymphal form is usually found spirally coiled within a cyst, the ventral surface corresponding as a rule to the convexity of the curve. In shape and structure the nymph closely resembles the adult, and the number of rings is the same.

Fig. 124.—Larva of Porocephalus armillatus. (*After Sambon.*)

Life history.—Little is known of the life history of *P. armillatus*; it is probably similar to that of the European linguatulid (*Linguatula tænoides*), which is also an occasional parasite of man. The ova, disseminated by snakes harbouring the adult form, reach the intermediary host probably with its food or drinking water, the larvæ encysting themselves in the liver, mesentery, or lungs. At a certain stage of development they escape from their cysts and migrate to the serous cavities, where they cause considerable inflammation. As a rule at this stage they are swallowed by their definitive host.

Pathogenesis.—There is much uncertainty as to the pathogeny of this parasite. Some consider it quite harmless. There can be no doubt as to the gravity of a heavy infection at the time when the parasites are migrating in their intermediary host. In Kearney's case, reported by Aitken, twenty or thirty parasites were found encysted in the liver and one or two in the lungs. The lungs were greatly congested. In Marchoux and Clouard's case the parasites were found in the liver and in the mesentery all along the intestine, but especially about the cæcum. In Chalmer's case numerous parasites were found moving freely in the abdominal cavity over the surface of the various organs. A large number were found within the lumen of the small intestine. Many were still encysted in the lungs.

The diagnosis of porocephalus infection is impossible.

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CHAPTER XLV

V. INTESTINAL PARASITES

I.—Nematodes

Microscopical examination of the fæces for ova of intestinal parasites.—If the fæces of the natives of warm climates, and of Europeans coming from warm climates, are systematically examined with the microscope, in a large proportion of cases they will be found to contain the ova of one or other of three species of nematode worms—*Ascaris lumbricoides*, *Trichocephalus trichiurus* (*T. dispar*), and *Ankylostomum duodenale*. The ova of the tapeworms and of the common threadworm (*Oxyurus vermicularis*) are rarely found in the stools, as these parasites do not, as a rule,

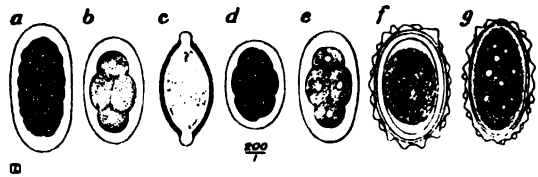

Fig. 125.—Ova of nematodes.

a, Strongylus subtilis; *b*, Ankylostomum duodenale; *c*, Trichocephalus trichiurus; *d*, Strongyloides stercoralis; *e*, Necator americanus; *f*, Ascaris lumbricoides; *g*, Ascaris lumbricoides (unfertilised).

part with their ova until the joints of the former, or the entire body of the latter, have left the alimentary canal; but as the three nematodes first mentioned pass their eggs directly into the bowel, these eggs habitually appear in the fæces and constitute unequivocal evidence of the presence of their respective parental forms. Occasionally the ova of hepatic and intestinal parasites—such as *Schistosomum japonicum*, *S. mansoni*, *Clonorchis sinensis*, *Fasciola hepatica*, *Fasciolopsis buski*, and other rare helminths are encountered; as these, with the exception of schistosomum, are very rare, from a practical point of view they may be disregarded. Without large experience the ova of the rarer parasites cannot be identified off-hand; but if the practitioner has learned to recognise those of the three common species, he will at once know when he comes across the ova of any of the rarer species, and, on referring to some special work on helminthology, will have little difficulty in arriving at a correct diagnosis.

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The microscopic examination of fæces for ova, though somewhat disagreeable, is by no means a difficult matter. All that is necessary, by way of preparation, is to place on the slip a minute portion of the suspected fæces—about the size of a hemp seed—and then to apply the cover-glass, gently gliding it over the slip so as to spread out the mass in a thin, fairly uniform, and transparent layer. If the bit of fæces prove too consistent, a little water may be added so as to soften it. If the stools are loose and watery, the sediment should be taken up with a pipette and examined. It is well to make two or three preparations. The microscopic examination must, in the first instance, be made with a low power—an inch, or better, a half-inch objective. Search must be made in every part of the slide, and every suspicious body carefully scrutinised, a higher power being used if necessary. A very little practice suffices for the identification not only of ova, but of the species of parasite to which the ova belong.

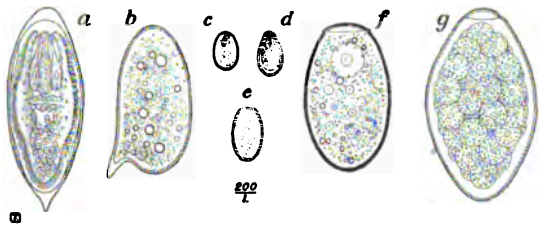

Fig. 126.—Eggs of Trematodes.

a, Schistosomum hæmatobium; *b*, S. mansoni; *c*, Heterophyes heterophyes; *d*, Opistorchis sinensis; *e*, Opistorchis noverca; *f*, Paragonimus westermani; *g*, Fasciolopsis buski.

The points to be attended to in the diagnosis of ova are size, shape, colour, thickness, roughness, smoothness, and markings on the surface of the shell; the presence or otherwise of yolk spheres, of a differentiated embryo, or, in the case of the cestodes, of the three pairs of embryonic hooklets; the existence of an operculum in the case of certain trematodes and of the broad tapeworms (*Dibothriocephalus*). The ova of the same species of parasite vary but slightly, and are in every instance sufficiently stable and definite for correct diagnosis.

Ova of Trichocephalus trichiurus (Fig. 125, *c*).—Of the three common nematodes mentioned—*Trichocephalus trichiurus*, *Ascaris lumbricoides*, and *Ankylostomum duodenale*—the ova of the first are most frequently met with. They occur sometimes in enormous numbers, as many as six or eight specimens being visible in one field of an inch objective. They form rather a striking object under the microscope. They are oval, measuring from 51–54 μ by 21–23 μ, the ends of the long axis of the oval being slightly pointed and tipped with a little shining projection or plug. Their general appearance suggests an

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elongated oval tray, the projections at the poles of the ovum representing the handles of the tray. They are dark brown in colour, sharply defined, doubly outlined, and contain no differentiated embryo.

The ova of *Ascaris lumbricoides* (Fig. 125, *f*, *g*) are considerably larger (60 to 75 μ by 40 to 58 μ) than those of *trichiurus* (Fig. 125, *e*). They are also, as a rule, more spherical, or, rather, more broadly oval; occasionally they are almost barrel-shaped. Like those of trichocephalus, they are dark brown in colour from bile staining, but they are much less sharply and smoothly defined, possessing a coarse thick shell which is roughened by many warty excrescences. The yolk contents are not always easily made out, nor, when made out, can any sign of embryo or segmentation be discovered.

In certain instances, supposed to be unfertilised, the ova are smooth on the surface, the rough outer layer being almost or altogether absent.

A point of practical importance to be attended to lies in the circumstance that the rough outer layer on the shell of the ovum of ascaris is very easily detached, leaving the egg with a sharp, smooth outline suggestive of some other species of parasite. To obviate this, in mounting fæces it is well to avoid too much gliding of the cover-glass over the slip.

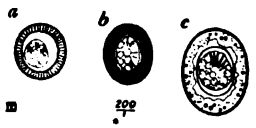

Fig. 127.—Eggs of cestoda. (*After Looss.*)
a, Tænia solium; *b*, Tænia saginata; *c*, Tænia nana.

The ova of *Ankylostomum duodenale* (Fig. 125, *b*) contrast very markedly with both the foregoing, particularly in the matter of colour. Trichocephalus and ascaris ova are invariably dark and bile-stained; those of the ankylostomum are beautifully clear and transparent. They measure 55 μ to 65 μ by 32 μ to 43 μ; have a regular, somewhat elongated oval form, with a delicate, smooth, transparent shell, through which two, or four, or eight light-grey yolk segments can be distinctly seen. It is well to search for these ova soon after the fæces have been passed; otherwise, owing to the rapidity with which, in favourable circumstances, development proceeds, the embryo may have quitted the shell and the egg be no longer visible.

TRICHOCEPHALUS TRICHIURUS (L.)

Synonyms.—*Ascaris trichiura. Trichocephalus hominis. T. dispar.*

Trichocephalus trichiurus, the whip-worm, lives principally in the cæcum. In many countries it is present in more than half the population. It is believed to maintain its position by transfixing, pin-fashion, with its long slender neck, a superficial fold of the mucous membrane. Wichmann claims to have shown, by serial sections of the cæcum at sites where

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the parasites were fixed, that it is merely embedded in the mucus between the intestinal villi. According to Powell, the females very much preponderate, the proportion to males being as 466 to 1. Except that the practitioner should be familiar with the appearance of its eggs in the stool, so that he may be able to distinguish them from those of ascaris, of ankylostomum, and of other parasites, the presence of *T. trichiurus* is of no practical moment. So far as known, it gives rise to no serious pathological lesion; a fortunate circumstance, seeing that hitherto it has been found impossible, with any degree of certainty, to dislodge it by anthelmintics.

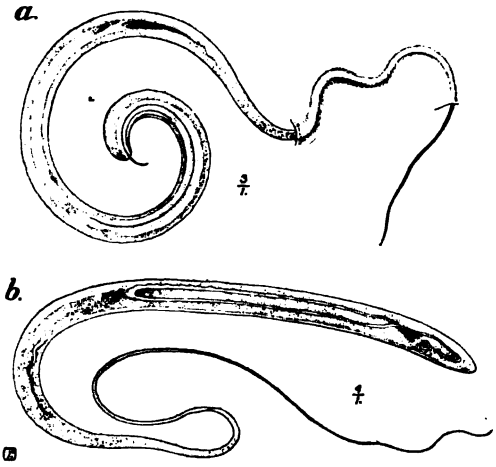

Fig. 128.—Trichocephalus trichiurus (magnified).
a, Male partly embedded in the mucous membrane of the intestine; *b*, female.

ASCARIS LUMBRICOIDES (L.).

Though not quite so common in tropical countries as trichocephalus, the ascaris is nevertheless very common indeed, especially in children, who often harbour these loathsome creatures in enormous numbers —in dozens, or even in hundreds. In those countries, at one time or another, nearly every child gets them; so much so that, when doubt exists about the nature of some obscure affection, a dose or two of santonin often produces results which will seem to justify a diagnosis of "worms," and, for the time being, perhaps satisfy an anxious mother.

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Mode of infection.—The reason for the great frequency of *Ascaris lumbricoides* in tropical countries is probably twofold—the warmth of the climate, and the habits of the people with regard to the disposal of night-soil. In the fæces the ova exhibit no trace of segmentation or of differentiated embryo; but if placed in water, or kept moist and in a warm place, in the course of from five or six months——longer or shorter according to temperature—the embryo is developed, and can be seen coiled up and moving about inside the egg-shell. If such an egg is accidentally or intentionally swallowed, on arrival in the stomach the shell is dissolved away and the contained embryo is set free. In a month it grows into a sexually mature animal, and, if both sexes are present, eggs in countless numbers are soon produced and appear in the fæces. Desiccation of the egg at atmospheric temperatures does not destroy the embryo, which will quickly revive on becoming moistened. In many warm countries night-soil is the favourite fertiliser, and is regularly collected and spread upon the fields. In this way the ova of ascaris obtain an opportunity of maturing, and thus, too, they have an opportunity of being swallowed by man. They may also be washed into drinking water; or, becoming desiccated on the drying up of the fields, be blown about as dust; or they may become attached to fruit or vegetables. In one of these, or in similar ways they finally reach the human stomach and there attain maturity.

Symptoms.—In many instances the ascaris gives rise to no very noticeable symptom; in other instances it is to be credited with a number of ill-defined gastric and perhaps nervous troubles—capricious appetite, foul breath, restless sleep, peevishness, vague abdominal pains, nausea, and so forth. Sometimes the worms get into the stomach and are vomited, their appearance giving rise to no inconsiderable alarm. They may even creep up the œsophagus and into the mouth, or out by the nostrils. Cases are on record in which they caused suffocation by wandering into the rima glottidis. They have

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been known to enter the bile-ducts and give rise to jaundice; to penetrate the intestinal wall and escape into the peritoneum, causing peritonitis; or to burrow into the abdominal walls and cause abscess. Fortunately these accidents are of rare occurrence; their possibility, however, should be borne in mind, and, apart from other obvious considerations, ought to make us endeavour to rid patients of these troublesome guests as soon as possible. With this object in view, it was my practice in China to give my little patients, as a matter of routine, a few doses of santonin twice a year; very often the precaution received its justification by the appearance of one or more ascarides in the stools.

Adults, especially young adults, although to a much smaller degree than children, are liable to entertain these verminous visitors. Sometimes certain obscure dyspeptic symptoms in grown-up people will resist all treatment until three or four grains of santonin and a purgative have been administered. I had a patient once who for a long time had been troubled with unaccountable nausea. One day, while he was sitting at breakfast, the feeling of sickness came on with unusual intensity. He had to leave the table, and, after one or two retching efforts, brought up an *Ascaris lumbricoides*. After this he was no more troubled with nausea. It is well, therefore, when puzzled over some obscure dyspeptic condition in tropical patients, to bear the ascaris in mind. If, for some reason, it is undesirable to give santonin unnecessarily, the stools ought first to be examined with the microscope. If ova (Fig. 125, *f*, *g*) are found, a dose or two of santonin may clear up diagnosis and cure the patient; if no ova are found, the drug may be withheld and the idea of ascarides abandoned.

Treatment.—The ascaris is readily expelled by a few grains of santonin. The dose is from half a grain to one grain for a child, three to five grains for an adult. A good plan of giving the drug is to prescribe three such doses on successive nights, the first and last dose to be followed by castor oil next

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morning. Patients, or mothers, ought to be warned about the peculiar effect santonin has on the urine and sometimes on the vision. I have only once seen any bad effects; in this instance a peculiar sort of intoxication, attended with delirium, which did not quite pass away for several days, followed its exhibition.

ANKYLOSTOMUM DUODENALE (Dubini) AND ANKYLOSTOMIASIS.

Synonyms.—*Anchylostomum duodenale. Anchylostoma duodenale. Strongylus duodenalis. Dochmius duodenalis. Uncinaria duodenalis.*

Ascaris lumbricoides, though an unpleasant parasite, cannot be considered a dangerous one, unless in very exceptional circumstances. It is otherwise with the ankylostomum which, in many countries, on account of the dangerous cachexia it gives rise to, called ankylostomiasis, amounts to a positive curse.

Nomenclature.—The form of endemic anæmia with which this parasite is associated is of so marked a character that it has received a variety of distinctive names. Thus, in the French West Indies, severe ankylostomiasis is known as *cachexie aqueuse*; sometimes as *malcœur*, or as *mal d'estomac des nègres*; in Colombia it is called *tuntun*, the sufferers being known as *tunientos*; in Brazil it has been called *oppilatio*, *opilaçao*, and *cançaço*; in Europe it is sometimes known as "miners' anæmia," or "tunnel disease," the latter in allusion to the notorious St. Gothard epidemic; the form occurring in Egypt is spoken of as Egyptian chlorosis; in Ceylon it has been called "beriberi," a name which has not infrequently caused confusion with true beriberi; and, doubtless, elsewhere there are local names for this peculiar verminous anæmia.

Geographical distribution.—Since its discovery by Dubini in 1838, the ankylostomum has been found so widely diffused that it may be said to occur in all tropical and subtropical countries. It occurs in Belgium, and has recently been

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found by Prof. Haldane to be the cause of an epidemic of severe anæmia in a Cornish mine. In northern countries it is rare; but it is abundantly present in the south of Europe, and in the tropical and sub-tropical regions of Asia and America; it has been ascertained to exist in North and South Queensland, Australia, and in several of the islands of the Pacific. So prevalent is it in many parts of India that, according to Dobson, quite 75 per cent. of the inhabitants are affected. In Egypt it is found at nearly every *post-mortem* examination; and there the anæmia it gives rise to is one of the most common causes for the rejection of recruits in the army. Thornhill regarded its ravages in Ceylon as far more serious than those of cholera; this, not on account of the number of deaths it causes directly, but on account of the vast numbers affected, the chronic nature of the disease, and the aggregate mortality, direct, and especially indirect, for which it is responsible.

Fig. 129.—Ankylostomum duodenale (natural size). (*Dubini.*) *a*, Male; *b*, female.

The parasite (Fig. 129). — The normal habitat of *A. duodenale* is the small intestine of man, particularly the jejunum, less so the duodenum, rarely the ileum or lower reaches of the alimentary canal; very occasionally it is found in the stomach. In these situations it attaches itself by means of its powerful buccal armature to the mucous membrane, from the blood of which it obtains a plentiful supply of nourishment. It is supposed to shift its hold from time to time, the abandoned bite continuing to ooze blood for a short period. It is said to be very prodigal of the blood it imbibes, the red corpuscles passing through its alimentary canal unchanged, the plasma alone being utilised.

The male and female ankylostomes—present generally in the proportion of one of the former to three of the latter—do not differ so much in size as is the case with many of the other nematodes. The male (Fig. 131) measures from 8 to 11 mm. in length by ·4 to ·5 mm. in breadth; the female (Fig. 130) 10 to 13 mm. in length by 1 mm. in breadth. Both sexes are cylindrical in form, white when they are alive, grey when dead, reddish brown when full of blood. In both sexes the posterior end is the broadest part, whence the body tapers forward to a narrow neck ending in a powerfully armed, bulging and distinct mouth capsule. The margin of this

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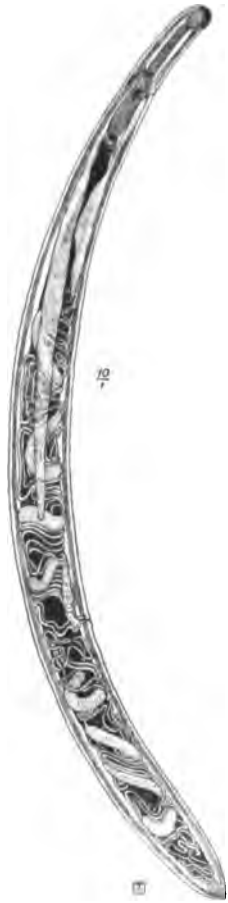

Fig. 130.—A. duodenale, female. (*After Looss.*)

Fig. 131.—A. duodenale, male. (*After Looss.*)

remarkable organ is furnished with four strong, claw-like hooks—two on each side of the ventral line, and two conical teeth—one on each side of the dorsal line. The tail of the female is conical, and ends in a short delicate spine; the anus being subterminal, and the vagina opening on the ventral surface at the commencement of the posterior third of the body.

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The tail of the male is provided with a large umbrella-like, trilobate bursa possessing eleven ribs. Two long and very delicate spicules project from the cloaca, which opens at the bottom of the bursa. Owing to the relative positions of the sexual openings, the worms in conjugation look like the Greek γ.

Reproduction and mode of infection.—The female ankylostomes produce a prodigious and never-ending stream of eggs (Fig. 125, *b*) which pass out in the fæces. As already stated, while in the body of the host the development of the embryo does not advance very far; but on leaving the human host it proceeds, in suitable circumstances, so rapidly that in one to two days a rhabditiform embryo (·2 mm. by ·014 mm.) is born. This minute organism (Fig. 133) is very active, voraciously devouring what organic matter it can find and, for a week, growing rapidly (to ·56 mm. by ·024 mm.). During this time it moults twice. After the second moulting it passes into a torpid condition, in which it ceases to eat, and growth is suspended. In this state it may live for weeks or months, moving about more or less languidly in muddy water, in mud, or in damp earth. Should chance so determine, it is finally transferred to the human alimentary canal, either in muddy drinking water, or in the mud or dirt adhering to the hands or the food dishes of the agriculturist, the brick-maker, or other operative engaged in handling the soil; or, it may be, in earth deliberately eaten by the geophagist and children. Arrived in its final host, after moulting again at the end of five weeks (Leichtenstern), it acquires sexual characters and the permanent adult form.

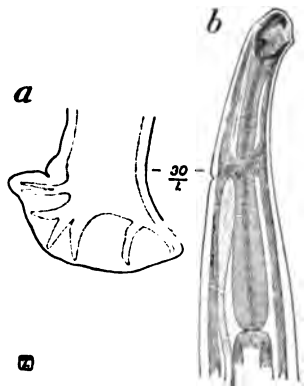

Fig. 132.—A. duodenale. (*After Looss.*)
a, Bursa; *b*, head.

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Until recently this was believed to be the only method of infection, but Looss has shown that the parasite may reach the intestinal canal by another route. In making some experiments with

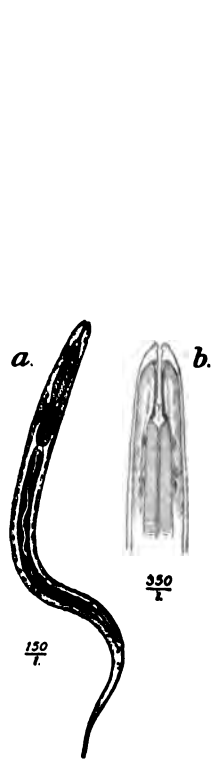

Fig. 138.—A. duodenale. (*Partly after Looss.*) *a*, Young larva; *b*, head.

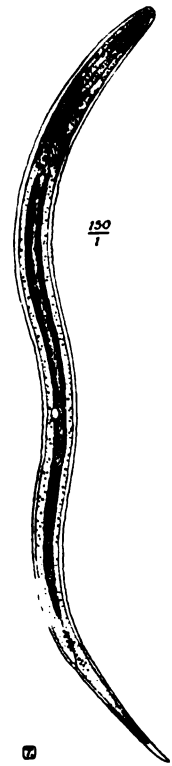

Fig. 134.—A. duodenale, mature lava. (*Partly after Looss.*)

"cultures" of ankylostoma larvæ, Looss inadvertently allowed the culture to come into contact with his hand. This was followed by redness and irritation of the skin of the part and, subsequently

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by well-marked ankylostomiasis; the sequence of events suggesting that the larvæ in the cultures had penetrated the skin of his hand and so attained the bowel. Subsequently Looss repeated this experiment on a human leg, an hour before its amputation. Sections of the skin showed the larvæ in the hair follicles, and some had traversed the hair papillæ and lay in the connective tissue around the follicles. Subsequently, other experiments on dogs and men have established the fact that the embryos of *A. duodenale* can enter the skin, and that they do so as a first step towards reaching the intestine. From the subcutaneous tissue they enter the blood-vessels and lymphatics, and by this channel are passively transferred to the lungs. Here they leave the capillaries, enter the air vesicles, and thence along the bronchi and trachea pass into the œsophagus and so to the stomach. It has been conjectured that during this passage the larva acquires the power of resisting the action of the gastric juice. If this be so, then the indirect route described must be the only way by which the ankylostome can arrive at maturity. The success of feeding experiments, which hitherto has been regarded as proof that the parasite passed directly to the stomach, may be attributed to the passage of the larvæ into the wall of the œsophagus while the dose of larva-laden material was being swallowed.

The duration of the life of *A. duodenale* in the intestine has not been determined; some state it in months, others in years (Sonsino)—one to three. On account of liability to reinfection, this point, an important one as affecting prognosis, is difficult to determine.

Giles holds that *A. duodenale* may become sexually mature while outside the human body and in the free state; in other words, that it is heterogenetic, an abundant supply of food favouring non-parasitic multiplication. His observations, supported by Ozzard, Annett, Ross and Sandwith, are opposed by Looss, who points out that probably other free-living nematodes have been mistaken for the species in

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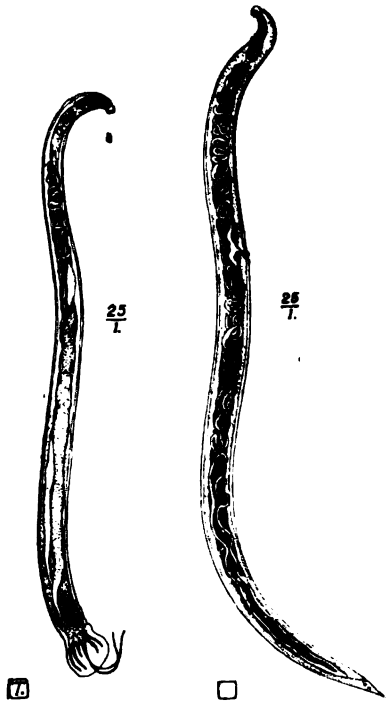
question; that in fact the illustrations in Giles's report represent three males belonging to different species and characterised by an entirely different configuration of the posterior extremity.



Male. Female.

Fig. 135.—Necator americanus. (*After Placencia.*)

NECATOR AMERICANUS (Stiles, 1902).

Synonym.—*Uncinaria americana.*

History.—In May, 1902, Stiles discovered that ankylostomiasis in America was not, as a rule, due to *Ankylostomum duodenale*, but to a new species of the closely allied genus *Necator*, which he named *Necator americanus.*

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Geographical distribution.—So far as determined, the distribution of *N. americanus* includes in America, Virginia, North and South Carolina, Georgia, Florida, Alabama, Texas, Porto Rico, Cuba, and Brazil. It has been found by Looss in pygmies from Central Africa, and by others in Assam, Burma, West Africa and elsewhere, suggesting that this species came originally from Africa or Asia.

Description of parasite.—It can be readily distinguished from *Ankylostomum duodenale*. It is a shorter and more slender worm. The male measures from 7 to 9 mm. in length by 0·3 to 0·35 mm. in diameter; the female 9 to 11 mm. in length

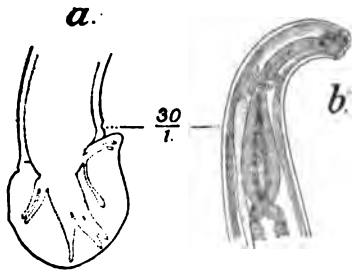

Fig. 136.—Necator americanus. (*After Looss.*)
a, Bursa; *b*, head.

by 0·4 to 0·45 mm. in breadth. The buccal capsule is much smaller, and presents an irregular border; instead of four ventral hook-like teeth, it has a ventral pair of prominent semilunar plates similar to those of the dog hook-worm, *Uncinaria stenocephala;* the pair of dorsal teeth is likewise represented by a pair of slightly developed chitinous plates of the same nature. The outlet of the dorsal head-gland, usually called dorsal rib or dorsal tooth, projects prominently in the oral cavity. Deep in the buccal capsule are one pair of dorsal and one pair of ventral sub-median lancets. The caudal bursa of the male presents a short dorso-median lobe, which often appears as if it were divided into two lobes. The

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dorsal ray is divided to its base, its two branches are prominently divergent, and their tips are bipartite instead of tridigitate, as in *A. duodenale.* The common base of the dorsal and dorso-lateral rays is very short. In the female the vulva is placed slightly in front of the middle of the body. The eggs are larger than in ankylostomum, they measure 64 to 75 μ in length by 36 to 40 μ in breadth.

Fig. 137.—Necator americanus, head. (*After Looss.*)

N. americanus inhabits the small intestine of man, and so far has not been found in any other part.

The life history of this worm has not yet been investigated; it is probably similar to that of *A. duodenale.*

ANKYLOSTOMIASIS.

History.—Although Griesinger had previously shown that Egyptian chlorosis was due to the presence of the ankylostomum in the small intestine, and although similar observations had been made on negroes in America, it was not until the very fatal epidemic of anæmia among the miners in the St. Gothard tunnel (in 1880) had called the attention of European observers to the subject, that the importance of this parasite as a pathogenic agent began to be properly apprehended. Multiplied observations have now shown that, although very minute, this blood-sucking parasite, if present in large numbers and for a length of time, more especially if its victims are poorly fed, is a very dangerous one indeed. The constant drain of blood which its presence entails, the catarrh arising from the irritation caused by the wounds it inflicts on the mucous membrane, the consequent impairment of nutrition, and, possibly, the absorption of some hæmolytic toxin—the product of the parasite—give rise to a grave cachexia, disqualifying to a greater or lesser extent the subject of it for work, and, not unfrequently,

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leading to a fatal issue. It is now recognised that many of the cases that were formerly regarded and diagnosed as "tropical anæmia" are cases of ankylostomiasis.

Its importance.—It is not in every instance in which the ankylostomum is present that consequences so serious ensue. There may be dozens of ankylostomes in the intestine without any appreciable anæmia, or, indeed, symptoms of any description whatever. Grave symptoms are the exception. One must be careful, therefore, to avoid concluding that the ankylostomum is the cause of every pathological condition with which it may chance to concur.

On the other hand, many inhabitants of tropical and subtropical countries are in a state of chronic starvation. Living on coarse, bulky, innutritious food, they are prone to dilatation of the stomach and dyspeptic troubles. In such, any additional cause of malnutrition, as a swarm of ankylostomes, and a daily though perhaps small loss of blood, may be sufficient to turn the scale against them. In those countries, as elsewhere, there are many who live just on the borderland between health and disease; to such the ankylostomum may prove the last straw that breaks the camel's back.

It may be that in some individuals with special susceptibility, some toxin developed by the parasite, just as in certain cases of *Dibothriocephalus latus* infection, produces a special type of anæmia.

It is evident that as a complication in typhoid, in kidney disease, in dysentery, in malaria, in fact in any chronic or exhausting disease, the importance of this anæmia-producing parasite cannot be ignored.

The practitioner in the tropics, therefore, must be constantly on the outlook in all cases of anæmia, of dyspepsia, and of debilitated conditions generally, for the ankylostomum. He must bear in mind that this parasite, as will be presently pointed out, if permitted to remain in the intestine for a length of time, may be the cause, not only of remediable anæmia, but of irremediable anæmia-produced degenerations of various organs. On this account, also, its early

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recognition becomes a matter of the first importance.

Further, ankylostomiasis is an important disease from the standpoint of the employer of native labour. The invaliding and inefficiency which it causes among coolies, not to mention the deaths, are often financially a serious matter to the planter and the mine-owner. To them, any wisely directed expense or trouble undertaken for the treating and controlling of this helminthiasis will be abundantly repaid by the increased efficiency of the labourer.

Symptoms.—The essential symptoms of ankylostomiasis are those of a progressive anæmia; an anæmia which is generally associated with dyspeptic trouble, but which, in uncomplicated cases, is not associated with wasting. If the progress of a case be unchecked, serous effusions in different organs and fatty degeneration of the heart ensue, and death may occur from syncope or from intercurrent complication.

One of the earliest symptoms of an extensive ankylostomum invasion is pain or uneasiness in the epigastrium. This is generally increased by pressure, but, for the time, may be relieved by food. The appetite, sometimes defective, is more often ravenous, though its gratification is apt to give rise to dyspeptic trouble of various kinds, to colic, to borborygmus, and perhaps to diarrhœa of imperfectly-digested food. Constipation may be present in some instances, irregularity of the bowels in others. The taste may be perverted, some patients exhibiting and persistently gratifying an unnatural craving for such things as earth, mud, lime—what is called pica or geophagy. The stools sometimes, though rarely, have a reddish-brown tinge from admixture of half-digested blood. Sometimes they may contain small flakes of blood-tinged mucus. Pure blood is rarely passed. An extensive hæmorrhage, unless there be concurrent colitis, is still more rare, although, *post-mortem*, considerable quantities of blood may be found in the small intestine. Fever of an irregular, intermitting, or even of a sub-continued type is common. On the other hand, the temperature may be constantly sub-

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normal. Or these conditions may alternate. After a longer or shorter time, symptoms of profound anæmia gradually disclose themselves. The mucous surfaces and the skin become pallid, the face is puffy, and the feet and ankles are swollen. All the subjective symptoms of a definite anæmia now become more and more apparent; there are lassitude, breathlessness, palpitations, tinnitus, vertigo, dimness of sight, mental apathy and depression, liability to syncope, and so forth. The circulation is irritable, and hæmic bruits can be heard over the heart and larger blood-vessels. Ophthalmoscopic examination may reveal retinal hæmorrhages.

From some of these symptoms, were it not that with the advancing anæmia there is no loss of weight, one might be led to suspect the possibility of tuberculous or cancerous disease, or of Bright's disease. So far from losing weight, the patient may appear quite plump and, though hæmocytometric estimates testify to a slow and steady fall in the corpuscular richness of the blood until the lowest limit compatible with life is reached, there is no true poikilocytosis as in idiopathic pernicious anæmia, no excessive leucocytosis as in leucocythæmia, and not necessarily any enlargement of lymphatic glands, liver, or spleen. There is generally a marked eosinophilia. The depression in the hæmoglobin value of the corpuscles is considerably greater than the fall in their numbers.

The rate of progress is very different in different cases. In some a high degree of anæmia may be attained, and even a fatal issue ensue within a few weeks or months of the appearance of the first symptoms. Such rapid cases are rare; more frequently the disease is an exceedingly chronic one, ebbing and flowing, or slowly progressing through a long series of years.

Should serious ankylostomiasis occur before puberty, the growth and development are apt to be delayed and stunted.

Diagnosis.—Provided its presence be suspected, ankylostomiasis is easily diagnosed. In tropical countries, in patients coming from tropical countries, and

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in miners who work in very warm mines in cooler climates, anæmia with concurrent eosinophilia should always suggest a microscopical examination of the fæces. If the ova (Fig. 125, *b*, *e*) of *A. duodenale* or of *N. americanus* are discovered, and no other reason for the anæmia be made out, the presumption is that one of these parasites is at the root of the mischief; at all events, no harm is likely to result from treatment based on this supposition. On the other hand, if no ova are found it must not be concluded that the case is not one of ankylostomiasis; for it sometimes happens that, in the later stages of the disease, symptoms will persist although the parasites which caused them in the first instance have disappeared spontaneously, or have been got rid of by treatment. Permanent degeneration of the alimentary canal, of the heart, liver, kidneys, and blood-forming organs may remain, and even prove fatal, although the primary cause is no longer present. The history and the absence of other sources of anæmia is all we may have to go upon in such circumstances.

Ankylostomiasis is sometimes confounded with beriberi, and *vice versâ*. The presence of paretic and cardiac symptoms not accounted for by the moderate degree of anæmia in beriberi, and their absence in ankylostomiasis, suffice for diagnosis. The anæmia of ankylostomiasis differs from that of malaria, inasmuch as the latter is accompanied by enlargement of the spleen, a sallow and perhaps pigmented complexion, an icteric tint of the scleræ, occasional attacks of well-marked periodic fever controlled by quinine, and, especially, the presence at such times of the malaria parasite in the blood. As an additional diagnostic feature, Rogers has pointed out that whereas in malaria the loss of hæmoglobin is in proportion to the loss of red blood corpuscles, in ankylostomiasis it is in excess of this. Of course, ankylostomiasis and malarial cachexia may concur, and often do concur, in the same individual.

Some idea of the intensity of the affection may be got from an enumeration of the eggs in a given

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quantity of fæces; according to Grassi and Parona, 150 to 180 eggs per cubic centigramme indicate an infection of about a thousand worms, male and female.

Pathological anatomy and pathology.—As already mentioned, the bodies of the victims of ankylostomiasis are not wasted; on the contrary, there is plenty of fat in the usual situations. The appearance of plumpness is further increased by a greater or lesser amount of general œdema. There may be effusions in one or more of the serous cavities. All the organs are anæmic. The heart is dilated and flabby, its muscular tissue being in a state of pronounced fatty degeneration. The liver, also, is fatty, and so are the kidneys.

If the *post-mortem* examination be made within an hour or two of death, the ankylostomes, in numbers ranging from a few dozens up to many hundreds, will be found still attached by their mouths to the mucous surfaces of the lower part of the duodenum, of the jejunum, and, perhaps, of the upper part of the ileum; but if the examination has been delayed for some hours, the parasites will have dropped their hold, and are then to be found lying in the mucus coating the inner surface of the bowel. Many small extravasations of blood —some fresh, others of long standing—are seen in the mucous membrane, a minute wound in the centre of each extravasation representing the point at which the parasite had been attached. Sometimes blood-filled cavities, as large as filberts, are found in the mucosa; each cavity enclosing one or two worms and, probably, communicating by means of a small hole with the interior of the intestine. Old extravasations are indicated by punctiform pigmentations. There may be evidence, in the shape of vesiculations and thickening of the mucosa, of a greater or lesser degree of catarrh. Occasionally, streaks or large clots of blood are found in the lumen of the bowel.

Daniels and others report that microscopic examination of the liver and kidneys shows the presence, within the cells of the parenchyma, of grains of yellow pigment having the reactions of hæmatoidin; indicat-

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ing an intravascular blood destruction, such as occurs in pernicious anæmia and other diseases in which excessive hæmolysis is a feature. On this account, and also because he finds granules of a ferrous nature in the liver cells, Daniels concludes that the anæmia in ankylostomiasis is, in a measure, the result of blood destruction within the vessels by some toxic substance produced by the parasite and absorbed from the bowel. These results have not been confirmed by all other observers; on the contrary, the late Dr. Beaven Rake concluded, from careful estimates of the amount of iron in the livers of five cases of ankylostomiasis, that in this disease the hepatic iron is below the normal average, and that the anæmia is entirely owing to the direct abstraction of blood by the parasites. Further observations are necessary before this question can be decided.

Treatment.—*Male fern.*—Until the introduction of thymol by Bozzolo in 1880, extract of male fern was the anthelmintic usually employed in ankylostomiasis.

Thymol.—Before the administration of thymol the patient should be put on liquid diet for a day or two, and have the bowels well cleared out by an aperient. In the morning, and following the action of the aperient, three or four ten- to thirty-grain doses of well triturated thymol, in cachets, in capsules, or in emulsion, are given on an empty stomach at intervals of an hour. If the bowels do not open spontaneously within four or five hours of the last dose an aperient should be given. Usually, by this treatment many ankylostomes are expelled and may be found in the motions. One such course of thymol may suffice; but it is well, after a week has elapsed, again to examine the stools microscopically, and, if it be found that ova are still being passed, to repeat the course of thymol once or oftener.

Certain precautions have to be observed in employing this drug. At times it gives rise to a very unpleasant form of intoxication—vertigo, excitement, etc., and the urine may become dark, as in carbolic

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acid poisoning. It is advisable therefore for the patient, while taking the drug, to keep his bed and to lie down for several hours after the last dose. Thymol is very insoluble in water, and is therefore, in ordinary circumstances, not readily absorbed in poisonous quantities; should, however, the patient, while thymol is present in the stomach, partake of any alcoholic drink, there is considerable risk of poisoning ensuing. Alcohol, ether, glycerine, turpentine, chloroform and oils are all solvents of thymol, and must therefore be avoided when this drug is being exhibited. Thornhill related an instance in which a fatal result was brought about, apparently, by neglect of the obvious precautions suggested by these facts. A man had received thirty grains of thymol in water at 7 a.m. "He experienced no special symptoms after it, and at 9 a.m. the nurse gave him a second dose of thirty grains. As this man was supplied with arrack as an extra, and as in such cases a portion of the arrack was usually given at 9 a.m., the nurse gave it to him just after administering the second dose of thymol. The result was that intense collapse set in almost at once, and, notwithstanding all efforts, the man died within twenty-four hours, the collapse manifestly being due to the arrack dissolving the thymol, which was thus absorbed." Thornhill mentions two additional fatal cases of thymol poisoning occurring in his experience; other writers have recorded similar fatalities. For this reason, and because it is an extremely unpleasant drug to take—sometimes giving rise to severe burning sensations in the stomach, throat and gullet, and, not unfrequently, to excitement, giddiness, fainting and vomiting—an equally efficient but safer drug is a desideratum.

Without careful preparation by rest and judicious feeding, thymol must on no account be used in advanced cases of ankylostomiasis or where prostration is extreme. It is contra-indicated in gastritis, dysentery, nephritis, and in active heart disease.

Beta-naphthol given in the same way as thymol, in doses of fifteen grains repeated every two hours

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for two or three times, is just as efficacious and less unpleasant.

Oil of eucalyptus thirty minims, chloroform forty-five minims, castor oil ten drachms, one half first thing in the morning, the other half thirty minutes later, is a very efficient vermifuge in ankylostomiasis, much less unpleasant and much less dangerous than any of the foregoing. It can be repeated for several days in succession. I have used this combination several times in Europeans who had on previous occasions taken thymol; they preferred the eucalyptus mixture.

Convalescence.—The dieting of convalescents from serious ankylostomum disease must, for a time, be very carefully conducted. In such, a rich, full dietary is to be avoided until the powers of digestion have become re-established; otherwise, enteritis and diarrhœa may prove very troublesome and retard recovery—perhaps prevent it altogether. Iron and arsenic are indicated as blood restorers.

Prophylaxis.—In devising a system of prophylaxis for ankylostomiasis, the fact that it is by means of the fæces of the already infected that the parasite is spread must be kept prominently in view. Fæcal contamination of the soil and water must therefore be prevented. The promiscuous deposition of fæces about huts, villages, and fields must be interdicted. Abundant and easily accessible privy accommodation must be provided in coolie lines, in miners' camps, in native villages, and along the highways of traffic. In the absence of a more elaborate system of conservancy, pits or trenches will suffice. They may be filled up with earth and fresh ones opened from time to time. I believe the Chinese plan of storing night-soil for months in large, cemented, water-tight pits is a good one. It is known that if the ova of the ankylostomum are kept in pure fæces the embryo is developed and escapes from the egg in due course; but it is also known that, unless the embryo be supplied with a certain amount of air and earth, it soon dies. The thing to be avoided, therefore, is the mixing of *fresh* fæces with earth. By the Chinese

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system the embryos of the ankylostomum are killed, and, at the same time, a valuable fertiliser is secured for the agriculturist.

It is manifest that in devising privies and sanitary regulations, the habits of the people they are intended to benefit must be taken into account; if this be not attended to, if native habits and prejudices are ignored, any system, no matter how perfect it may be in theory, will fail in practice.

The water supply should also be carefully guarded from all possible sources of fæcal contamination. Drinking water should be boiled or strained. So far as possible, facilities for removing all earth and mud from the hands and dishes before food is partaken of should also be provided and their use encouraged.

Badly contaminated ground had better be abandoned. If this should be found impracticable, the soil should be turned over with the plough, or roasted with grass fires, or treated in such a manner that any ova or embryos it may contain are destroyed or buried. The systematic periodical inspection of plantation coolies is to be recommended. At these inspections, all subjects of anæmia or dyspepsia should be put aside for more careful examination; if the ova of ankylostomes are found in their fæces a judicious dosing with some of the drugs mentioned may avert serious disease in the individual, and also prevent him from becoming a source of danger to his companions.

In view of the great danger to health that exists in certain countries from this and similar parasites, the sanitary authorities in such places ought to circulate among the people, by means of printed leaflets or posters, a few simple directions for the prevention of ankylostomiasis and kindred diseases.

Recently attempts have been made in Porto Rico to reduce or exterminate the ankylostomiasis so prevalent in that island. Special officers have been detailed for the purpose, whose duty it is to submit the entire population to systematic drugging with beta-naphthol. The result in the improvement of the health of the islanders, and increase in the aggregate

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labour capacity, has been most encouraging. This is an example of sanitary energy which we might follow with advantage in our own West Indian possessions and elsewhere.

ANKYLOSTOMUM DERMATITIS.

A form of dermatitis affecting the feet of coolies on plantations in Assam, in the West Indies, and probably elsewhere in the tropics, and variously known as ground itch, pani-ghao, water itch, water pox, water sores, sore feet of coolies, has recently been ascribed by Bentley to the penetration of the skin by ankylostoma larvæ. This disease is of much economic importance to the planter.

The soil in the neighbourhood of coolie lines is extensively contaminated by fæcal matter. During rainy weather the ankylostoma ova in the fæcal materials are hatched, and the larvæ escape into, and possibly multiply in, the damp earth. The bare feet of the coolies are constantly soiled with this larva-laden earth, and in this way, in many tropical plantations, Looss's experiment is unintentionally carried out on a large scale. Dermatitis, vesiculation, and it may be pustulation or even extensive ulceration, and probably ankylostomiasis anæmia ensue. The services of the affected coolie are lost to the planter till the irritation or ulceration subsides and the anæmia is cured.

Bentley's suggestion has been contradicted by Dalgetty, Stiles and others. Looss also points out that the symptoms of ground itch do not tally with those caused by the penetration of ankylostomum larvæ through the skin. Perhaps coolie itch may not in every instance be produced in this way, but undoubtedly it is so in a proportion of cases. A patient of mine, a sugar planter, who at that time knew nothing about the ankylostomum, observed that an attack of coolie itch in any of his labourers was sure to be followed by anæmia. He assumed that the skin trouble was the cause of the anæmia, and that the former was produced by a micro-organism picked up from the soil. He made his coolies, on going out

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to their work in the morning, walk through a bucket of Barbados tar, and then through a heap of sand, with the result that coolie itch and anæmia ceased on his estate.

Personal cleanliness and the use of some form of foot covering during the wet season, together with the prophylactic measures for ankylostomiasis already mentioned, are the special preventive means indicated as against this disease. As regards treatment, antiseptic foot baths and some soothing ointment are indicated.

Œsophagostomum brumpti (Railliet and Henry, 1905).

History.—This parasitic nematode was discovered by Brumpt, in 1902, at the *post-mortem* of a thirty-year old Pouma negro on the River Omo, Africa. Six immature females were found within cyst-like nodules in the wall of the cæcum and colon. The new parasite belongs to the sub-family *Sclerostominæ*, of the family *Strongylidæ*, and to the genus *Œsophagostomum*, several species of which are found in the domesticated animals (cattle, sheep, hogs). The genus is also distributed among *Tapiridæ*, *Edentata*, and *Quadrumana*. We know already a number of species from the Quadrumana. They have been found in the gorilla, in the ourang-outang, in the chimpanzee, and in various monkeys belonging to the genera *Cercopithecus*, *Cynocephalus* and *Macacus*.

Description of parasite.—The young females found by Brumpt varied in length from 8·5 to 10·2 mm. and presented a maximum breadth of 295-325 μ. The cuticle is transversely striated; the anterior extremity exhibits the ovoid cuticular expansion characteristic of the genus, limited anteriorly by a salient oral ring (oral vestibule) and posteriorly by a constriction which is especially marked on the ventral surface and 200 μ distant from the oral vestibule. The posterior extremity of the worm tapers gradually to a caudal point slightly bent dorsally. The oral vestibule is provided with a crown of twelve sharp chitinous plates directed forwards and inwards, and bears six papillæ, two lateral and four submedian. The œsophagus is club-shaped and measures 470-500 μ in length by 150 μ in its widest diameter. Anteriorly, it opens into the oral capsule with three slightly recurved teeth

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about 8 μ long, which fit into three corresponding indentures of the posterior border of the oral capsule. Posteriorly, it presents a three-lobed valve. The intestine runs almost in a straight line to the anus, which opens at 170-200 μ from the posterior extremity. The vulva is placed anteriorly to the anus at 350-475 μ from the caudal end. Neither anus nor vulva is marked by any prominence of the body wall.

The ova of *Œ. brumpti*, like those of other parasites belonging to this genus or to the closely allied genus *Sclerostoma* probably, hatch in water and by this medium reach a fresh host, penetrating either through the œsophagus or the skin. They finally settle beneath the intestinal mucosa, usually between the ileo-cæcal valve and the anus, and here grow considerably in size, feeding on the blood of the host. Having practically reached the adult stage, they leave their cysts for the purpose of copulation and oviposition, and they and their eggs are expelled with the fæces.

Life history and pathogenesis.—The allied species, *Œ. columbianum*, which, according to Curtice, is frequent in adult sheep in the south of the United States and is more particularly observed in the autumn and winter, does not appear to cause any serious trouble except when present in great numbers. The parasite may be found in its adult state within the lumen of the cæcum or colon, but it is found more frequently in the larval stage lodged beneath the mucous membrane in cysts varying in size from that of a pin's head to that of a hazel-nut, each cyst containing a coiled-up worm. The species peculiar to apes and monkeys are likewise found during their larval stage within small hæmorrhagic cysts beneath the mucosa of the cæcum and large intestine. The parasites are blood-suckers; their intestines are crammed with erythrocytes. The larger cysts usually present a small perforation at their summit; through this the worm protrudes and escapes. *Œ. dentatum*, which inhabits the pig, the wild boar, and the white-lipped peccary (*Dicotyles labiatus*), is found not only in the cæcum and colon, but also further up in the small intestine, and Von Linstow found it within the liver. According to Baillet, the eggs of this species hatch in water within three or four days and the liberated embryo measures 200-250 μ.

STRONGYLOIDES STERCORALIS (Bavay).

Synonyms.—*Anguillula stercoralis, A. intestinalis, Leptodera stercoralis, L. intestinalis, Rhabdonema intestinale.*

It sometimes happens that while searching the fæces for the ova of the ankylostomum, the observer is astonished by seeing a small, snake-like animal (Fig. 139) suddenly rush across the field of the microscope. On careful examination, this animal is found to be about 0·2 mm. or 0·3 mm. in length by 0·013 mm. in breadth; to have a sharply pointed tail and a rounded head; to be transparent; and to exhibit a short œsophagus which terminates in a double œsophageal bulb, the

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posterior end of which is provided with three tooth-like segments. This is the larval form of *Strongyloides stercoralis.*

Strongyloides stercoralis was discovered by Normand in 1876. For a time it was supposed to be a cause of a form of chronic diarrhœa very prevalent in Cochin China. Later investigations, while clearing up the natural history of the parasite, have robbed it of any claim to pathological importance. It has been found that, though not so common, its geographical distribution is about coextensive with that of *Ankylostomum duodenale*, and that the physical conditions demanded for the

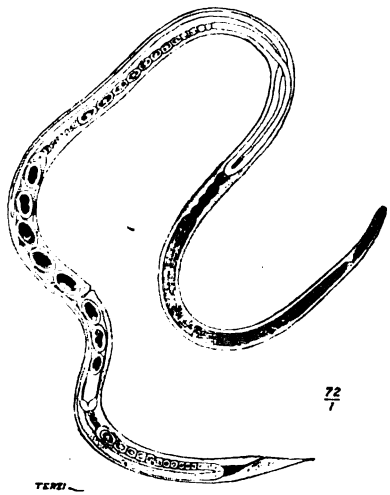

Fig. 138.—Strongyloides stercoralis, female. (*After Looss.*)

non-parasitic stages of these two worms are about the same. Powell found it in India in about fifteen out of every twenty cases of anæmia.

The mature strongyloides (Fig. 138) is a minute, slender worm, measuring 2–3 mm. in length by ·06 mm. in breadth. No male parasite has been discovered. The adult female is readily recognised by her dimensions, and by the string of five or six ellipsoidal eggs (·01 mm. by ·034 mm.) visible about the centre of the body.

As Kanazy has shown, the parasite bores deeply into the mucous membrane of the intestine, and frequently into the epithelium of Lieberkühn's glands, both for nourishment and oviposition. The eggs develop in the intestinal wall, so that before leaving the host, unless during violent purgation, the larva has escaped and is swimming about in the fæces, as

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already described, with great vigour, especially when these are fluid. Only in the event of violent purging do the ova appear in the stools. Such ova (Fig. 125, *d*) are readily recognised by the way in which they are strung together, end on end, inside a delicate tube. On leaving the host, unless they have access to some non-putrefying fluid, the larvæ soon die; it is necessary, therefore, if we would follow their further development, to mix the fæces with water. If this mixture be kept at a low temperature the young rhabditiform larva develops into a filariform larva which, on reaching its host, assumes the

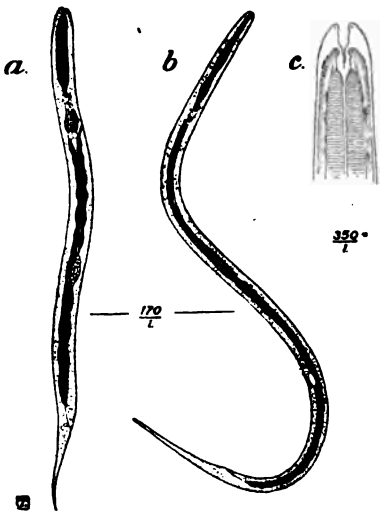

Fig. 139.—Strongyloides stercoralis. (*Partly after Looss.*)
a, Young larva from fæces; *b*, mature larva; *c*, head.

mature parasitic form already alluded to. If, on the contrary, the cultivating medium be kept at a higher temperature, the larvæ develop into male (·7 mm.) and female (1·0 mm.) rhabditic forms which, in time, produce in their turn filariform larvæ, similar to those obtained directly from the embryo in cold climates, and capable, on being swallowed by man, of developing into mature *Strongyloides stercoralis*.

This parasite must undoubtedly produce considerable irritation of the bowel, but its pathogenic *rôle* has not been definitely ascertained. It is usually present in large numbers, and has been found occasionally coiled up in the intestinal follicles. The larvæ may pierce into the lacteals and have been found in the blood. Van Durme has shown that, like the larvæ of

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Ankylostomum duodenale, the filariform larvæ of strongyloides may penetrate through the skin. Hitherto the use of anthel-

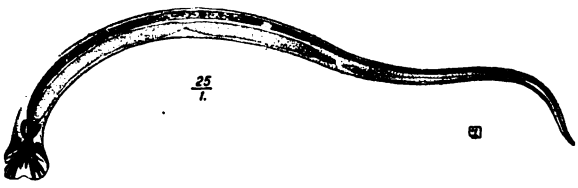

Fig. 140.—Strongylus subtilis, male.

mintics has not proved effectual in procuring their expulsion. Sonsino recommends the prolonged exhibition of liquor ferri perchloridi in combination with small doses of thymol.

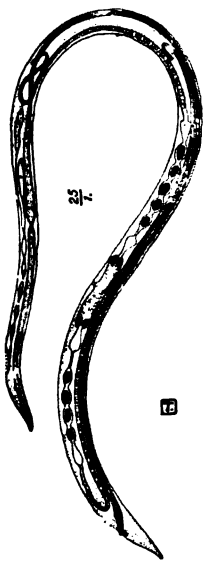

Fig. 141.—S. subtilis, female.

Fig. 142.—S. subtilis, bursa. (*After Looss.*)

The prophylaxis for rhabdonema is the same as that recommended for *Ankylostomum duodenale*.

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STRONGYLUS SUBTILIS (Looss).

Looss has described a very delicate nematode frequently encountered in Egyptian fellahs. It has since been found by Ijima in Japan. Its habitat is the upper part of the small intestine. The male, which is provided with two spicules, is from 4 to 5 mm. in length by 0·07 mm. in breadth; the female is slightly larger and is much more abundant than the male. The eggs are oval, thin-shelled, with an unsegmented vitellus, and measure 63 μ by 41 μ. This parasite does not occur in large numbers; and, as its mouth is unarmed and its dimensions are exceedingly minute, it does not appear calculated to give rise to any particular symptoms.

GNATHOSTOMUM SIAMENSE (Levinsen, 1889).

Synonym.—*Cheiracanthus siamensis.*

History. *Gnathostomum siamense* was discovered by Deuntzer in Bangkok (Siam) and described by Levinsen, who proposed to call it *Cheiracanthus siamensis.*

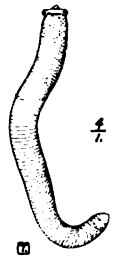

Fig. 143.—Gnathostomum siamense. (*After Levinsen.*)

Geographical distribution.—So far it has been seen in Siam only. It was met with in three patients, one of whom had five or six of these worms.

Specific diagnosis. – Only one female specimen was preserved and forwarded to Levinsen. It measured 9 mm. in length by 1 mm. in breadth. The cephalic extremity, slightly narrower than the rest of the body, had the appearance of a sucker bordered by two lips and was surrounded by eight rows of hooklets. The posterior extremity terminated in a three-lobed prominence, at the base of which the anus opens. The anterior third of the body was beset with tridentate spines, followed by scattered simple spines, which gradually became smaller and then disappeared entirely. The vulva opened a little behind the middle of the body.

Life history and pathogenesis.—We know nothing of the life history of *Gnathostomum siamense.* Other species of the genus live in the stomach of various vertebrates. Before attaining maturity, they are found in cysts beneath the mucosa. *G. spinigerum* is found in various kinds of wild cats (*Felis catus, F. concolor, F. tigris*). Lewis found it in the pariah dogs of Calcutta. *G. hispidum* lives in the stomach of hogs. Fedtschenko found it in a Turkestan wild hog and in a Hungarian domestic hog. Csokor found it in hogs slaughtered at Vienna, Strose in Bakony's hogs, and Collin in cattle in Germany. In Vienna butchers have long known this parasite under the name of "three-coloured worm." The parasite described by Levinsen came from a young Siamese woman, who presented a livid and painful tumefaction of the breast

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with slight fever. Rounded nodules the size of beans appeared at the seat of inflammation, beneath the skin. From one of these nodules the gnathostomum protruded.

II.—Trematodes.

PARAMPHISTOMUM WATSONI (Conyngham, 1904).

Synonyms.—*Amphistomum watsoni*, *Cladorchis watsoni*.

History.—This parasite was found in 1904 by Watson in the duodenum and upper part of the jejunum of a negro patient from German West Africa, who died of starvation and diarrhœa. The stools were numerous, watery, and of a bilious colour, and contained many yellow, translucent, oval trematodes. At the *post-mortem* the jejunum was found to be full of these trematodes, some of them alive and still adherent. The mucosa showed no hæmorrhages, but appeared to be slightly congested. The other parts of the bowel, as also the other organs, were normal.

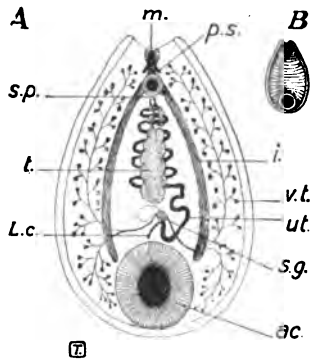

Fig. 144.—Paramphistomum watsoni. (*After Shipley.*)
a, Magnified; *b*, natural size.

Description.—*P. watsoni* (Fig. 144) is of a reddish brown colour and measures 8 to 10 mm. in length by 4 to 5 mm. in breadth; it is oval in shape. The oral sucker is small; the ventral sucker or acetabulum large and at the posterior extremity of the body. The genital pore opens at the anterior end of the ventral surface on a level with the bifurcation of the intestine. The ova measure 125 μ in length by 75 μ in breadth.

Life history.—We know nothing of the life history of this parasite, but probably it is similar to that of *P. cervi*, the conical fluke of cattle and sheep, which was thoroughly worked out by Looss in 1896. The eggs of *P. cervi* contain a ciliated embryo (miracidium) which escapes from the eggshell under the stimulus of light and moisture. Swimming about in the water, which it must necessarily reach for further

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development, it penetrates into the visceral cavity of certain snails (*Physa alexandrina*, *P. micropleura*), and in these develops and multiplies parthenogenetically. In about two months, having attained the so-called *cercaria* stage, its progeny escape from the snail, swim around in the water and finally encyst themselves on plants or other objects. The final host (cattle, sheep, etc.) is attained either through drinking water or pasture.

Geographical distribution.—Information is as yet very scanty, but there is reason to believe that *P. watsoni* is by no means uncommon in certain parts of Northern Nigeria, where it gives rise to serious intestinal trouble, especially in children. A patient who had lived there for some time told me that on one occasion, being seized with violent diarrhœa, he passed about a pint of material containing innumerable moving bodies which he described as resembling the heads of tadpoles, doubtless specimens of *P. watsoni*.

Treatment.—As for adult tapeworms.

GASTRODISCUS HOMINIS (Lewis and McConnell, 1876).

Synonym.—*Amphistoma hominis.*

History.—This parasite was described by Lewis and McConnell in 1876 from two sets of specimens, the first procured from O'Brien and Curran, who found them in the vicinity of the ileo-colic valve at the *post-mortem* of an Assamese in Gowhatty; the second belonging to the Pathological Museum of the Calcutta Medical College, and presented in 1857 by Simpson, who found them in the cæcum and ascending colon of an Indian who died from cholera in the Tirhoot gaol hospital.

Fig. 145. — Gastrodiscus hominis. (Nat. size.)

Geographical distribution.—We know little of the geographical distribution of *G. hominis*; it is probably widely distributed throughout Asia, and appears to be rather common in India. Law found it in an East Indian immigrant in British Guiana.

Description of the parasite.—It is of a reddish colour in fresh specimens, and measures 5 to 8 mm. in length by 3 to 4 mm. in breadth. Its body is divided into an anterior

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rather slender conical portion, and a posterior flattened ventrally concave disc; the oral sucker is small, ventral; the acetabulum is at the posterior border of the ventral disc. The genital pore opens at about the middle of the anterior portion on a level with the bifurcation of the intestine. The testicles are two in number and lobate; the vas deferens very sinuous. The eggs are oval and measure 150 μ by 72 μ; they are operculated.

Pathogenesis. — *G. hominis* is found in the cæcum and colon. The mucous membrane is marked with numerous red spots resembling leech-bites. These spots are caused by the parasites, which, attaching themselves to the mucosa by means of their suckers, produce minute pimple-like elevations of the surface. When the parasites occur in great numbers they cause much irritation.

Life history.—Probably as in *Paramphistomum cervi.*

Treatment.—The same as for adult tapeworms.

FASCIOLOPSIS BUSKI (Lankester, 1857).

Synonyms.—*Distoma buski, Dicrocœlium buski.*

History.—*Fasciolopsis buski* was first described by Busk in his "Diseases of the Liver," published in London in 1845. Busk found this parasite in 1843 in the duodenum of a Lascar who died at the Seamen's Hospital.

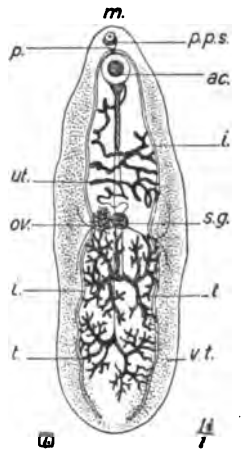

Fig. 146.—Fasciolopsis buski. (*After Odhner*)

Geographical distribution.—*F. buski* is an Asiatic trematode; it has been found in India, Assam, the Straits Settlements, Sumatra and China.

Specific diagnosis.—It is the largest trematode inhabiting man. It measures 24 to 40 mm. or more (75 mm. according to Busk) in length by 12 to 14 mm. in breadth. In shape it is an elongated oval, rather narrower anteriorly than posteriorly, with flat ventral surface, slightly convex dorsal surface, and very thin margins. It has a smooth skin without

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spines. The oral sucker (0·5 mm. in diameter) is subterminal and placed on the ventral surface. The ventral sucker is larger (1·6 to 2 mm. in diameter) and placed close to the oral. It is prolonged into a kind of sac (2 to 8 mm. long) directly under the ventral surface. The pharynx (0·7 mm. long) is preceded by prepharynx (0·28 mm. long); the œsophagus is very short and the intestinal cæca are simple and present two characteristic curves towards the middle line, one at about the middle of the body, the other between the testes. The genital pore opens on the median line immediately anterior to the ventral sucker. The testes are in the posterior half of the body, one posterior to the other; both are branched dichotomously. The ovary is branched, and is placed about the middle of the body on the right of the median line. The vitellaria are well developed, and extend from the ventral sucker to the caudal end of the body, where they meet. The acini are very small. The eggs are numerous and measure 120 to 130 μ in length by 77 to 80 μ in breadth. They are closed, I find, by a very delicate operculum.

Pathogenesis and treatment.—This parasite inhabits the upper part of the small intestine. In two recorded instances (Cobbold) it was associated with attacks of recurring diarrhœa and other signs of intestinal irritation. The best treatment is thymol or eucalyptus oil, given as in ankylostomiasis.

FASCIOLOPSIS RATHOUISI (Poirier, 1887).

Synonym.—*Distomum rathouisi.*

History.—*Fasciolopsis rathouisi* was passed by a Chinese woman and preserved by Rathouis, a missionary at Sikawei, Shanghai. It was first described by Poirier in 1887. Most authors consider this species identical with *F. buski*, but Moniez (1896) questioned their identity, and Odhner's (1902) recent work seems to prove that the two forms are distinct.

Specific diagnosis.—*F. rathouisi* measures 25 mm. in length by 16 mm. in breadth. In shape it is oval; the anterior extremity is produced into a more or less distinct, short cephalic cone. The oral sucker is subterminal and very small (0·5 mm. in diameter), the ventral sucker is much larger (2 mm. in diameter) and situated at about 2 mm. from the oral sucker. The testes are situated side by side in the posterior half of the body. The vitellaria do not meet at the back. The eggs measure 150 μ in length by 80 μ in breadth.

Nothing is known of its life history.

HETEROPHYES HETEROPHYES (Bilh. v. Sieb., 1852).

Synonyms. — *Distomum heterophyes, Dicrocœlium heterophyes, Distoma heterophyes, Heterophyes ægyptiaca,*

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Mesogonimus heterophyes, Cœnogonimus heterophyes, Cotylogonimus heterophyes.

History.—*Heterophyes heterophyes* was discovered in 1851 in Cairo by Bilharz at the *post-mortem* of a child.

Geographical distribution.—It has been reported from Egypt and Japan, and probably has a wide distribution.

Zoological distribution.—Looss has found it in Egypt in the dog (*Canis familiaris*), in the cat (*Felis domestica*), in a fox (*Canis niloticus ?*) and in a kite (*Milvus parasiticus*). Janson reports it from the intestine of the dog in Japan.

Specific diagnosis.—*H. heterophyes* (Fig. 147) is the smallest trematode, so far as we know, inhabiting man. It measures 1 to 1·7 mm. in length by 0·3 to 0·7 mm. in breadth. It has an oval, elongate shape and a reddish colour. The neck is not sharply defined from the body, and may be greatly outstretched. The oral sucker (0·09 mm. in diameter) is subterminal and about one-third the size of the ventral sucker (0·23 mm.), which is placed at about the middle of the body. The cuticle is thickly beset with quadrate scales, 5 to 6 μ long by 4 μ broad. The pre-pharynx is short (80 μ in length); the pharynx measures 50 to 70 μ in length by 40 to 50 μ in diameter. The œsophagus is about three times as long. The intestinal cæca extend to the posterior extremity, where they converge and terminate close to the excretory bladder. The lateral ends of the vitellaria extend beyond the intestinal cæca. The genital pore opens postero-laterally to, and in the immediate vicinity of the ventral sucker; it is surrounded by a muscular ring. Testicles oval, in extreme posterior end of body. Ovary globular, median and anterior to the testes. Receptaculum seminis as large as the ovary; uterine coils not numerous, and extending between the ventral suckers and the testicles. Eggs light brown, thick-shelled, oval, 20 to 30 μ by 15 to 17 μ; contain a ciliated embryo when oviposited.

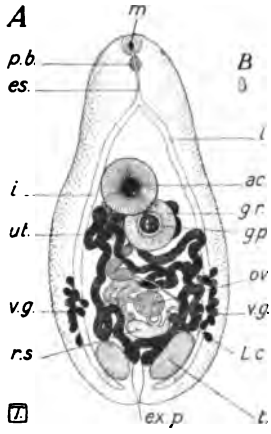

Fig. 147.—Heterophyes heterophyes. *a*, Greatly magnified; *b*, natural size.

Life history.—Not determined.

Pathogenesis.—It seems to have little pathological importance. It inhabits the small intestine.

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III.—Cestodes.

The ordinary tape-worms, *Tænia saginata* and *Tænia solium*, and their respective cystic forms, are common enough in the tropics and sub-tropics, their distribution being regulated by the presence or absence of their proper intermediary hosts—the ox in the one case, the pig in the other—and by the habits of the people as regards cooking and conservancy. *Echinococcus granulosus* (= *Tænia echinococcus*) of the dog, and its cystic form—hydatids—are found wherever the dog and sheep are found, that is practically everywhere. The broad tapeworm (*Dibothriocephalus latus*) is known to occur in Turkestan, in Japan—where the natives are in the habit of eating raw fish—in Madagascar, and among the natives on the shores of Lake 'Ngami, South Africa. Ichthyophagous habits are probably responsible for the occurrence of *Diplogonoporus grandis*, another large Dibothriocephalid found by Ijima and Kurimoto in a Japanese from the province of Higen.

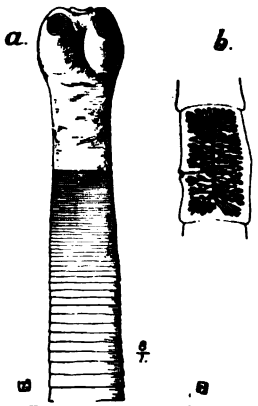

Fig. 148.—Tænia saginata (magnified). (*After Braun.*)
a, cephalic end; *b*, mature segment (nat. size).

The only cestodes of man which, so far as is known, have any claim to be regarded as more or less special to warm climates are *T. africana*, *T. hominis*, *Hymenolepis nana*, *Davainea madagascariensis*, *D. asiatica*, *Sparganum mansoni* and *S. proliferum*. Doubtless there are other species which so far have escaped observation.

TÆNIA AFRICANA (Linstow, 1900).

History.—*Tænia africana* was described by Linstow in 1900 It was found in German East Africa, in native soldiers stationed at Langenburg, near Lake Nyassa.

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Specific diagnosis.—*T. africana* differs considerably from the common unarmed tapeworm of man. Its strobila attains 1·4 metres in length, and is composed of about 600 proglottides. The scolex is quadrilateral, unarmed, very small (1·38 mm. broad by 0·47 mm. long), and is provided with an apical sucker (0·16 mm.) in addition to the usual four suckers (0·63 mm.). The neck is very short, and somewhat broader than the scolex. The proglottides are all broader than they are long. Immediately at the back of the scolex they measure 0·16 mm. in length by 1·78 mm. in breadth and 0·59 mm. in thickness, about the middle of the strobila they are 3 mm. long by 9 mm. broad and 1·20 mm. thick. The terminal and gravid strobila are 7 mm. long by 12 to 15 mm. broad and 1·35 mm. thick. The genital pores alternate irregularly, and are placed in the middle of the border of each segment. The testicles are very numerous and scattered throughout the

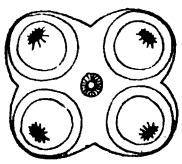

Fig. 149.—Tænia africana. (*After Linstow.*)

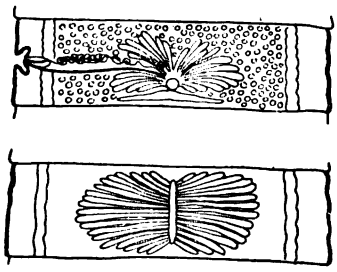

Fig. 150.—Tænia africana.
A, Frontal section of mature segment.
B, „ „ gravid „

middle layer. The vas deferens is much convoluted. The cirrus pouch is pyriform and thick-walled. The cirrus and vagina are beset with bristles directed outwards. The receptaculum seminis is fusiform. The ovary consists of two fan-shaped wings, composed of club-shaped tubes centering towards the shell-gland; the latter is median and globular. The uterus includes a median stem and 15 to 24 lateral, unramified branches, which are longer than the stem, and spread out like a fan. The ova are spherical, the embryophore 31 to 39 by 33·8 μ, with thick radially-striated shell; hooks of the onchosphere measure 7·8 μ in length.

The cystic stage of this tapeworm is unknown. Linstow suggests that it may be found in the zebu (*Bos indicus*), the flesh of which the natives are in the habit of eating raw.

TÆNIA HOMINIS (Linstow, 1902).

History.—*T. hominis* was described by Linstow in 1902, from a specimen obtained from the intestine of man in Aschabad, Asiatic Russia.

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Specific diagnosis.—The strobila examined by Linstow was immature, it measured 70 mm. in length. The scolex measured 1·34 mm. in length by 2 mm. in breadth, and exhibited a rudimentary unarmed rostellum. At the back of the suckers there was a characteristic circular ridge. The genital organs were not developed.

The cystic form is unknown.

Fig. 151.—Tænia hominis, head. (*After Linstow.*)

HYMENOLEPIS NANA (v. Siebold, 1852).

Synonyms.—*Tænia nana, Diplacanthus nanus, Hymenolepis murina.*

History.—This minutest of the tapeworms inhabiting man was first found as a human parasite by Bilharz, in Cairo, in 1851. The following year it was described by von Siebold, who proposed to call it *Tænia nana.* In 1887, Grassi identified it with *Hymenolepis murina* of the rat, and showed that it can dispense with an intermediary host, the larva penetrating into a villus of the rodent's intestine to become a cysticercoid, and then re-entering the canal to become transformed into the adult stage.

Zoological distribution.—*H. nana* is found in the brown rat (*Mus decumanus*), black rat (*M. rattus*), house mouse (*M. musculus*), dwarf field mouse (*M. minutus*) and garden dormouse (*Eliomys quercinus*).

Geographical distribution.—It is found in Egypt, Siam, Japan, the southern States of the American Union, Brazil, Argentine and throughout Europe, but more especially in the warmer parts, as in Sicily where, according to Calandruccio, 10 per cent. of the children are affected.

Specific diagnosis.—The strobila varies in length from 5 to 45 mm. with the number of proglottides, which are usually from about 100 to 200. The scolex is subglobular and measures 139 to 480 μ in diameter; it is provided with a well developed rostellum armed with a single crown of 20 to 30 hooklets 14 to 18 μ long; the suckers are globular and have a diameter of 80 to 150 μ. The neck is long. The proglottides are very short anteriorly, further down the chain they increase in size but remain broader than long. Only the hindermost

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segments may equal or even slightly exceed their breadth. The maximum breadth of the proglottides is from 0·5 to 0·9 mm. The genital pores open on the left margin near the anterior border of each segment. There are three testes in each segment, the vas deferens widens to form a seminal vesicle within the cirrus pouch. The gravid uterus occupies nearly the entire segment. The eggs number from 80 to 180 in each proglottis; they are oval or globular, and present two distinct membranes; the outer one measures from 30 to 60 μ in diameter, the inner one from 16 to 34 μ. The latter exhibits at each pole a more or less conspicuous mamillate projection.

Development.—The development of *Hymenolepis nana* has been worked out experimentally by Grassi in the rat. The egg is swallowed and after hatching enters a villus in the lower part of the small intestine (Fig. 152), where it transforms into a *cercocystis*.* The six-hooked embryo is found concysted from 24 to 50 hours after ingestion, its long axis corresponding to that of the villus, and the posterior end bearing the embryonal hooks directed towards the lumen of the intestine. Occasionally two parasites may be found in the same villus.

Fig. 152.—Hymenolepis diminuta.

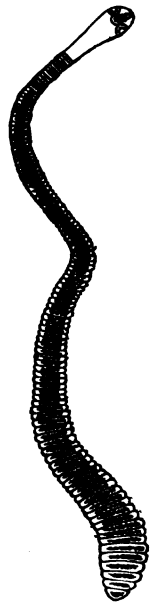

Fig. 153.—Hymenolepis nana. (Magnified.)

In about 40 to 70 hours after ingestion the scolex has appeared, and in 80 to 90 hours after ingestion the rostellum is provided with hooklets. Then the parasite passes into the lumen of the intestine, where it can be seen attached to the epithelium of the villus with short neck and no trace of segmentation. The rapidity of development varies somewhat, and, as a rule,

* The term *cercocystis* was introduced by Villot to designate those cysticercoids which are provided with caudal appendages.

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various stages are found occurring simultaneously in the same host. Strobilisation is rapid, the proglottides attain maturity in about 10 or 12 days, and about 30 days after infection the eggs of the parasite begin to appear in the fæces. These never develop in the same host unless reintroduced *per os* or through a reverse peristalsis, because, as in *Oxyuris vermicularis*, the embryo will not hatch unless the egg be subjected to the action of the gastric juices. Young white rats proved most susceptible to the infection, whilst rats already harbouring the parasites were refractory. Grassi's observations do not entirely disprove the possible agency of an intermediary host as in other tapeworms, but they certainly show that it can be dispensed with and, indeed, that as a rule the rat acts both as definitive and intermediate host. Experiments in man were not conclusive. Out of eight persons fed with eggs or mature segments of the parasite both from man and rats only one became infected. This occurred, however, in a region (Catania) where many harbour this tapeworm.

Pathogenesis.—*H. nana* is very minute, but as a rule it occurs in large numbers—usually hundreds, not infrequently thousands. When attached to the intestine it fixes its rostellum deeply into the lumen of a Lieberkühn's follicle, thus altering and destroying many of the epithelial cells. It is obvious, therefore, that a number of these worms must give rise to considerable irritation and possibly favour secondary infection. According to Grassi, *H. nana* may bore deeply into the mucosa, and at the *post-mortem* of a case in which 400 specimens were found in the ileum, Visconti and Segré noticed that the mucosa throughout the small intestine was tumefied, hyperæmic, and covered with a thick layer of greyish mucus, through which the worms were scattered The most frequent symptoms reported by authors are abdominal pain, which may or may not be associated with diarrhœa; convulsions of various sorts, frequently epileptiform; headache and strabismus The nervous phenomena are ascribed to the absorption of toxic products elaborated by the parasite. On account of its small size this parasite is easily overlooked. Diagnosis is based on the presence of the characteristic ova in the fæces. Some care is requisite in looking for the eggs because, owing to their transparency, they may escape observation.

Treatment.—*H. nana* is readily expelled by

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male fern. If a patient harbours this parasite he should not be allowed to sleep in the same bed with another person. On prophylactic grounds rats and mice should be banished from the house, and all food kept out of their reach.

DAVAINEA MADAGASCARIENSIS (Davaine, 1869).

Synonyms.—*Tænia madagascariensis, T. demerariensis.*

History.—*Davainea madagascariensis* was first described by Davaine in 1869 from fragments of two strobila without heads sent to him by Grenet, who discovered it at Mayotte, Comoro Islands, in two Creole children. In 1891 Leuckart described an entire specimen with scolex which was sent to him from Siam. But it is chiefly to Blanchard that we owe our knowledge of this parasite.

Geographical distribution.—The first two cases published were those of Grenet in Mayotte, but both came from abroad. One of them was an eighteen months' old child who had arrived from the Antilles five months previously, the other a little two year-old girl from Réunion who had landed two months previously. The next four cases were seen at Port Louis (Mauritius) by Chevreau, who looked for the parasite at Blanchard's suggestion. All these cases occurred in children, two of whom were only five years old. The seventh case, published by Leuckart, occurred at Bangkok (Siam) in a three-year-old boy, the son of a Danish sea-captain. The eighth was that of Daniels, who discovered the worm in an adult native in Georgetown (British Guiana). A further specimen was described by Blanchard, who found it in Davaine's collection with the following label: "Nossi-Bé (Island), November, 1873; passed by a little girl three years old."

Zoological distribution.—As yet *D. madagascariensis* has only been found in man, but the genus is widely distributed in mammals and birds. Amongst mammals it is found in rats (*Mus siporanus, Mus rajah*), in hares (*Lepus sylvaticus, L. arizonæ, L. melanotis*), in the pangolin (*Manis pentadactyla*). Amongst birds it is found in the ostrich (*Struthio camelus*), the common rhea (*Rhea americana*), the emu (*Dromæus novæ hollandiæ*), the little egret (*Ardea garetta*), the grey parrot (*Psittacus erithacus*), and in fowls, pigeons, turkeys, pheasants, partridges, grouse, woodpeckers, blackbirds, starlings and quails.

Specific diagnosis.—The strobila attains 25 to 30 cm. in length by 1·4 mm. in breadth, and is composed of 500 to 600 proglottides. The scolex is provided with four large round suckers and a retractile rostellum surrounded by a double crown of 90 hooklets 18 μ long. The rostellum when invaginated forms a kind of pouch which gives it the appearance of an apical sucker. In the two specimens examined

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no hooklets were seen round the suckers, and in one the rostellum was unarmed. This may be on account of the caducity of the hooks. The neck is very wide, thick, depressed antero-posteriorly and furrowed laterally. The proximal segments are broader than long, the distal longer than broad (2 by 1·4 mm.). The last 100 proglottides are gravid and form one-half the length of the entire strobila. They resemble apple seeds in shape. The genital pores are unilateral and open near the proximal corner of each segment. The cirrus pouch is fusiform, the ductus ejaculatorius very long and sinuous, the testicles over 50 in number. The receptaculum seminis is unusually long and broad; it extends to the middle of the segment and communicates with the oviduct. The uterus is composed of a number of tubes rolled up on each side into an almost spherical coil. When filled with ova, the windings of the uterus unroll and extend throughout the proglottis; they then lose their walls, so that the eggs come to lie free in the parenchyma. The eggs then become surrounded, singly or in small groups, by parenchymatous cells forming egg-balls, of which from 300 to 400 may be present in each segment. The globular onchosphere (8 μ to 15 μ) is surrounded by two perfectly transparent shells, the outer one bearing two pointed projections.

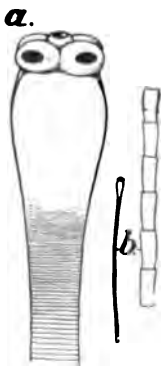

Fig. 154.—Davainea madagascariensis. (*After Blanchard.*) *a*, Head; *b*, nat. size.

The cystic stage is unknown. Blanchard suggests that it might be found in cockroaches (*Periplaneta orientalis*, *P. americana*, etc.). He points out that the parasite has a wide distribution within the tropics, and that cases of infection have occurred in islands, in seaports and on board ship. The cockroach is cosmopolitan in distribution, it infests ships and contaminates food. Other tapeworms of the genus Davainea are known to spend their larval stage in insects and molluscs. According to Grassi and Revelli, some of these tapeworms, as, for instance, *D. proglottina* of fowls, may dispense with an intermediary invertebrate host and spend both their larval and adult stages within the body of the same host.

Pathogenesis.—We know nothing of the pathogenesis of this form of tæniasis. The parasite has been found almost exclusively in young children.

DAVAINEA ASIATICA (Linstow, 1901).

Synonym.—*Tænia asiatica.*

History.—*Davainea asiatica* was described by Linstow in 1901, from a specimen in the Zoological Museum of the Imperial Academy of Science in St. Petersburg. It was

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passed by a man in Aschabad (Asiatic Russia, near the northern frontier of Persia), and preserved by Anger.

Specific diagnosis. — The specimen examined by Linstow measured 29·8 cm. in length, and is composed of 750 segments. The scolex is missing. The proglottides are all broader than long, measuring 0·16 mm. in width at the proximal end, and 1·78 mm. at the distal end. The posterior margin of each segment extends over the anterior margin of the next following segment. The genital pores are unilateral and open in the proximal third of each proglottis. The testicles (35 to 44 μ in diameter) are arranged in a ventral and dorsal layer of about eight rows each. The vas deferens extends in convolutions about $\frac{1}{3}$ across the segment; the cirrus pouch is pyriform; the ovary extends across the segment between the ventral canals. The vagina forms a large fusiform receptaculum seminis. The uterus breaks up into 60 to 70 egg-balls in each segment. Mature eggs were not observed.

The cystic form is unknown.

Fig. 155. — Davainea asiatica sagittal section of gravid segment. (*After Linstow.*)

INTESTINAL MYIASIS.

A residence in the alimentary canal of some vertebrate animal is a regular feature in the life history of many dipterous insects. The ova of the insect are either licked from the skin, or swallowed in the food on which they had been deposited. In this way they get transferred to the stomach where, after a time, the larva is hatched out and proceeds in development. In due course it appears in the fæces. Man is not unfrequently victimised in this way, especially in tropical countries. Sometimes, until a correct diagnosis is arrived at, not a little alarm is caused by the appearance of these creatures in the stools. They are easily recognised. The ringed, cylindrical body, from $\frac{1}{2}$ inch to 1 inch in length according to species, broad at one end, tapering at the other, and usually beset with little spines or hairs, is sufficiently diagnostic (Fig. 156).

Already we know over twenty species of diptera whose larvæ have been found in, or expelled from the human intestinal canal. In Europe the majority of cases of intestinal myiasis, a not infrequent

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occurrence, are caused by *Homalomyia canicularis* (a fly closely resembling the common house fly and erroneously considered a young form of the latter on account of its smaller size), and the closely related *H. scalaris.* Austen believes that intestinal myiasis, due to the larvæ of these flies, is probably to be traced to the parent flies having oviposited on the anus when the patient has been using some country privy where such insects are common.

Fig. 156.—Larva of Calliphora vomitoria.

A dose of castor oil will probably suffice to expel any of these creatures that may not have been passed spontaneously.

A rational prophylaxis would consist in the covering up of food after it has been cooked, in order to prevent the access of flies.

Instances in which the larvæ have been discharged *per urethram* have also been met with, though more rarely.

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SECTION VI.—SKIN DISEASES

CHAPTER XLVI

DISEASES OF THE SKIN

I.—Non-Specific

PRICKLY HEAT

Prickly heat or, as it is sometimes called, lichen tropicus, is probably a form of miliaria (not of lichen) connected with the excessive sweating incident to the heat of tropical climates. According to Pollitzer, the mechanism of its production depends on the non-cornification of the cells of the stratum corneum, the individual cells of which, in consequence of their being sodden by constant perspiration, swell and so obstruct the orifices of the sweat glands, thereby leading to accumulation of sweat in the ducts. Pearse regards the disease as an acute distension of the sebaceous glands by their own secretion; the glands, he holds, are over-stimulated in order to supply an adequate amount of sebum to the skin, so as to make up for the loss of that material washed away by inordinate sweating. Durham regards prickly heat as an infective disease produced by a minute and very active amœba, readily found in the fluid of the vesicles provided search is made before the contents become turbid.

Nearly every European in the tropics suffers from prickly heat, particularly during the earlier years of residence. Some never seem to become acclimatised in this respect, but continue year after year to exhibit their crop of prickly heat when the hot season comes round.

Though sufficiently annoying in the robust and

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healthy, in them prickly heat is not a grave affair. It is otherwise in the case of the invalid, of delicate sickly children, of hysterical and, especially, of parturient women; to these it may prove, by interfering with sleep and provoking restlessness, a very serious matter. Prickly heat is also a common though indirect cause of boils; for the breaches of surface, following on the scratching it induces, afford many opportunities for the invasion of the micro-organisms of that disease.

Prickly heat consists of a miliary-like eruption, generally most profuse on those parts of the body, as around the waist, which are closely covered with clothing; but it also occurs on the backs of the hands, arms, legs, forehead, occasionally on the face, the scalp, in fact on any part of the surface of the body except the palms and soles. The minute, shining, glass-like vesicles, and the numerous, closely set and slightly inflamed papules, give the skin the feeling as if thickly sprinkled with grains of sand. The eruption may keep out for months on end, becoming better or worse according to circumstances. The pricking and itching are often exceedingly distressing. Anything leading to perspiration immediately provokes an outburst of this almost intolerable itching — nothing more certainly than a cup of hot tea or a plate of hot soup. Long drinks, exposure to the hot sun, close rooms, warm clothing, all aggravate the distress. Sometimes the little vesicles may pustulate, doubtless from micrococcus infection. So soon as the weather becomes cool the eruption and the irritation quickly subside.

Treatment.—Manifestly the most important thing is the avoidance of all causes of perspiration —particularly the copious consumption of fluids, especially hot fluids—moderation in exercise, avoiding close rooms, warm clothing, and so forth. Soap should not be used in the bath. The sleeping mattress and pillow should be covered with a finely woven grass mat, and the bed provided with what is known in the East as a "Dutch-wife"—that is, a hollow cylinder, 4 feet by 8 or 10 inches, of open rattan

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work, over which the arms and legs can be thrown and unnecessary apposition of sweating surfaces so avoided. A punkah at night is a great comfort. Many things have been recommended as preventives; for example, rubbing the body over after the bath with the juice of a lemon, Jeyes' fluid or bran in the bath, etc. Every bath-room in the tropics should be provided with some mildly astringent and antiseptic dusting powder. A very good one consists of equal parts of boric acid, oxide of zinc, and starch. This should be freely applied, after careful drying of the skin, particularly to the axillæ, crutch, under the mammæ in women, and between the folds of skin in fat children and adults. A simple precaution of this sort saves much suffering both from prickly heat and epiphytic skin disease.

Durham recommends painting the patches with weak iodine or, better, rubbing in solution of corrosive sublimate, 1 in 500 to 1 in 1,000: this he found very efficacious, curing the disease with certainty after one or two applications. He suggests the use of some form of obstetric soap as being less liable to lead, through inadvertence, to accidental poisoning.

Pearse strongly recommends the inunction of a mixture of almond oil and lanoline in the proportion of 8 to 1, and scented according to fancy. St. George Gray finds thin flannel a better wear than cotton or linen as a preventive of prickly heat. Sometimes the following powder, gently rubbed in for five or ten minutes with a damp sponge, cures bad patches of prickly heat: Sublimed sulphur, 80 parts; magnesia, 15 parts; oxide of zinc, 5 parts. Lotions of calamine, with or without hydrocyanic acid, or of carbolic acid, relieve the itching temporarily.

II.—Caused by Bacteria.

Tropical Sloughing Phagedæna.

Definition.—A rapidly spreading, but generally, after a time, spontaneously arrested gangrene of the skin and subjacent tissues, resulting in the formation

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of a large sloughing sore. Though occasionally fatal, these sores, as a rule, under favourable conditions, granulate and cicatrise, or become chronic ulcers.

Geographical distribution. — Sloughing phagedæna is common in most tropical countries, particularly in those with a hot, damp climate. These sores are often named after those districts in which they are specially prevalent; thus we hear of Mozambique ulcer, Yemen ulcer, etc. They are found principally in jungle lands, less frequently in towns and well-settled districts. Whether tropical sloughing phagedæna and hospital gangrene, at one time so prevalent in the hospitals of Europe, are the same disease, it is difficult to say. They agree in some respects; but in the marked tendency of the tropical sore to self-limitation, and, possibly, as Scheube points out, in its relatively feebly infective power, there is some indication of a specific difference.

Ætiology.—Doubtless depending on the proliferation in the affected tissues of some specific micro-organism, not yet satisfactorily separated, the germ of sloughing phagedæna finds its special opportunity in the bodies of men who from overwork, underfeeding, exposure, malaria, dysentery, scorbutus, and the like, are physically depressed. Thus it is apt to attack the half-starved, malaria-stricken pioneers in jungle lands, overdriven slave gangs, and soldiers campaigning in the tropics. In such circumstances a slight wound, an abrasion, even an insect bite, or an old chronic ulcer may serve as the starting-point for one of these terrible sores. Where yaws and sloughing phagedæna are co-endemic, the sores of the former may become infected with the virus of the latter, and serious sloughing and cicatricial contractions result. The feet and legs, being most exposed to injury, are the most frequent locations for this form of ulceration; but the arms or any other part of the body may also be attacked.

Symptoms.—If the disease occur in previously sound skin the first indication is the formation of a large bleb with sero-sanguinolent contents. The formation of this may be attended with some pain

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and constitutional irritation. When, in the course of a few hours, the bulla ruptures, an ash-grey, moist slough is exposed. The sloughing process rapidly extends in all directions until the skin and subcutaneous fascia, over an area many inches in diameter, are converted into a yellowish, moist, horribly stinking slough. After a few days the centre of the slough begins to liquefy, the sore still continuing to extend at the periphery. In the course of a week or longer the sloughing process may cease and the slough be gradually thrown off. Then it is seen that not only have the skin and superficial fascia been destroyed, but that possibly muscles, tendons, nerves, vessels, and even the periosteum of the bones have shared in the gangrenous process. Fortunately in many instances the deeper structures are spared, the disease being relatively superficial. Sometimes, however, important structures, including joints, bones and large blood-vessels, are destroyed; in such cases, even if life be spared, great deformity may ensue from different forms of ankylosis, or from strangulation of a distal part by a contracting cicatrix.

When the disease attacks a pre-existing wound or sore, the granulating surface of this becomes dry, and rapidly assumes the appearance and characters of a slough.

In sloughing phagedæna the neighbourhood of the sore is somewhat congested and swollen, particularly so if the patient has been obliged to use the limb. Constitutional disturbance may be considerable and of an adynamic type. On the other hand, it occasionally happens that large sores are attended with singularly slight local or general reaction. In bad cases a sapræmic condition is apt to supervene and carry off the patient; or death may occur from bleeding from the opening of a large blood-vessel.

Treatment.—It is of the first importance to endeavour to correct any cachectic state which may be present. Thus good food, fresh vegetables, lime-juice, and quinine are almost invariably indicated. Opium in full doses, not merely to assuage pain, but on account of its special action on the phagedænic

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process, is usually of great service. Locally, an endeavour must be made effectually to destroy the germ by the application of some powerful and penetrating caustic to the diseased surface. With this view, on the strength of considerable experience, I recommend that the patient be put under chloroform and the slough thoroughly dissolved off by the free application of pure carbolic acid, a piece of lint on a stout stick being used as a mop for the purpose. Thereafter the limb should be elevated and placed under some improvised irrigator from which a weak, warm antiseptic solution should continuously trickle over the now clean surface. If the phagedænic action recur the carbolic acid must be promptly reapplied as often as may be necessary. On healthy granulations springing up the ulcer is to be treated on ordinary principles.

Patients with this disease should be regarded as infective, and, so far as possible, isolated.

BOILS.

The anatomical and clinical features of this painful affection are too familiar to require detailed description. Suffice it to say that a boil is produced by the proliferation of *Streptococcus pyogenes aureus*, *Torula pyogenica*, or other pyogenic micro-organisms in the skin and subcutaneous tissue; that the organism gives rise to local and limited infiltration of the tissues with lymph which subsequently and rapidly dies, the necrotic core being surrounded by an areola of acute inflammation; that this core is separated by a process of sloughing and so got rid of, the resulting ulcer speedily healing and leaving a depressed scar, which, when occurring about the legs, may become pigmented. Though a self-limiting disease locally, it is nevertheless capable of being inoculated elsewhere in the same individual, both through a breach of surface and, also, by simple contact of the discharges with the skin, the micro-organism apparently entering by a hair follicle. This auto-inoculability of boils is apt to be overlooked.

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Conditions of debility, presumably by lowering resistance, predispose to boils; the subjects of diabetes are specially prone to them, the saccharine state of the blood or secretions seeming to be particularly favourable to growth of the specific germ.

Few Europeans in the tropics escape an attack of boils at one time or another. In some instances crop after crop succeed one another, the individual boils being so numerous that the patient is quite unfitted for work by the attendant pain and fever. In certain years so many members of a community are attacked that the disease may be described as being epidemic. These epidemics, occurring when some particular fruit is in season, are very generally, but probably incorrectly, attributed to the use of the particular fruit in question. Mangoes, probably erroneously, are frequently held responsible.

Treatment.—Any constitutional irregularity must be treated appropriately. Malaria demands quinine; anæmia and debility, iron and wine; constipation, aperients; diabetes, a suitable diet. I have never seen any good from such vaunted specifics as calcium sulphuret, tar water, or yeast.

Boils ought never, unless in very exceptional circumstances, to be poulticed. Poulticing, although it may relieve the pain of the existing boil, is prone to be followed by more boils in the area sodden by the heat and moisture. Neither should boils be incised or squeezed. The only exception to the rule for not cutting is in the case of boils occurring in the scalp or in the axilla. In the former situation, unless opened early, they are apt, especially in young children, to burrow and cause troublesome abscesses; in the latter situation boils tend to be very indolent and painful, and do not readily spontaneously break through the lax integuments.

In any situation in which the boil is liable to be irritated by pressure or clothing, it is sometimes a good plan to cover the part with a circle of washleather spread with soap plaster, and having a small hole cut in its centre corresponding to the apex of

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the boil. When a boil opens, the discharge must be kept from soiling the adjoining skin, and the patient must be warned against touching the skin elsewhere with pus-soiled fingers. The parts must be frequently cleansed with 1 in 1,000 corrosive sublimate lotion, powdered with boracic acid and covered with a dry, absorbent antiseptic dressing. A threatening boil may often be aborted by touching the little initial itching or vesiculated papule with some penetrating antiseptic, as iodine tincture, or by painting it with collodion. A very successful method is to drill slowly into the centre of the papule with a pointed pencil of hard wood dipped in pure carbolic acid. The point of the pencil should penetrate at least an eighth of an inch, and should be frequently recharged with the acid during the drilling process; the pain is trifling. In this way, in a severe attack of furunculosis, boil after boil may be aborted and the attack brought to an end. In obstinate chronic furunculosis excellent results have attended treatment conducted on Wright's method of exalting the opsonic index of the blood.

In severe cases change of air may be necessary.

PEMPHIGUS CONTAGIOSUS.

Definition.—A non-febrile, highly contagious skin disease peculiar to warm countries. It is characterised by the formation of large vesicles or bullæ which are unattended by marked inflammation, ulceration, or the formation of crusts or scars.

Geographical distribution.—Pemphigus contagiosus is very common in South China during the hot weather; in some years it may be described as being epidemic. It is perennial in the Straits Settlements, and it is known in Madras, in North Queensland, Japan, and America. Doubtless, although it has escaped notice by most medical writers, it is common enough elsewhere in the tropics, or wherever heat and moisture combine to bring about a state of skin favouring its development on the infective material being applied. It is especially common in schools and similar institutions

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where large numbers of children are thrown much together; they readily pass the disease one to the other. European children are more prone to it than native children; European adults are by no means exempt, but the native adult is rarely affected.

Symptoms. — Pemphigus contagiosus closely resembles certain forms of the impetigo contagiosa of temperate countries, and is doubtless a variety of this class of skin disease. The individual lesions, as can readily be ascertained by inoculation experiments, begin as minute erythematous specks, which rapidly proceed to the formation of vesicles, bullæ, or even large pemphigus-like blebs. The little blister springs abruptly from sound skin; there is no, or very little, areola of congestion. For a short time the hemispherical bleb is beautifully pellucid, tense, and shining. Presently the serous contents become somewhat turbid, and the blister gets flaccid and dull. At this stage, either from scratching or pressure, the blister is generally ruptured. The morbid process does not at once come to an end, but proceeds as an advancing, eccentrically-spreading exfoliation of the epidermis; an exfoliation which may not cease to advance until an area an inch or more in diameter is denuded of epithelium. Then, in that particular spot, the disease stops, a pinkish, slightly glazed-looking patch, rarely covered with a tissue paper-like scale, remaining for some time. Occasionally, after the rupture of the primary bleb, vesication may continue in the peripheral portion of its remains. Only one or two blebs may be visible on the entire surface of the body; generally there are many, the disease being spread by the fingers in scratching or rubbing.

Pemphigus contagiosus may occur in almost any part of the body. In young children it is usually diffuse; in adults it is mostly confined to the axillæ and crutch. In these situations it gives rise to much irritation and discomfort, owing to the successive crops of bullæ running into each other and rendering the parts raw and tender, and predisposed to boils or some form of eczematous intertrigo.

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During warm, moist weather it may be kept up indefinitely by auto-inoculation.

Assistant-Surgeon Soorjee Narain Singh describes a series of cases of a form of contagious pemphigus occurring in rapid succession in the children of three families in India (exact locality not specified), which bears some resemblance to the pemphigus contagiosus above described. It differs, however, inasmuch as in the Indian disease the bullæ were very large—often larger than hen's eggs, and persisted for from one to three weeks. In one of the thirteen cases described there followed a certain amount of sloughing at the seat of the bullæ; in the others there was neither ulceration nor constitutional disturbance.

Ætiology and pathology.—Like ordinary impetigo contagiosa, this is undoubtedly a germ disease. I have found a diplococcus in the epidermis and fluid of the blister; whether this is the special bacterium responsible for the disease, cultivation and inoculation experiment have not yet decided. The Leishman body has been found in the contents of the blebs. Its presence there has probably no ætiological significance so far as this special lesion is concerned.

Diagnosis.—Absence of constitutional symptoms, or a history of such, distinguishes pemphigus contagiosus from chicken-pox. Absence of trichophyton elements and of a well-defined, slightly raised, festooned and itching margin, together with the presence of large blebs and scaling of the epidermis, distinguish it from ordinary forms of body ringworm—a disease with which, when occurring in the armpits and crutch in adults, it is frequently confounded.

Treatment.—Cleanliness, the frequent use of a bichloride of mercury lotion (1 to 1,000), and a dusting powder of equal parts of boracic acid, starch and zinc oxide are speedily effective. In the school and nursery those responsible for the care of children must be informed of the contagiousness of this unpleasant affection, and measures be instituted accordingly.

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III.—Caused by Vegetable Parasites.

MYCETOMA.

Definition.—A fungus disease of warm climates, affecting principally the foot, occasionally the hand, rarely the internal organs or other parts of the body. It is characterised by enlargement and deformity of the part; an oily degeneration and general fusion of the affected tissues; the formation of cyst-like cavities communicating by sinuses, and containing peculiar mycotic aggregations in an oily purulent fluid which escapes from fistulous openings on the surface. The disease runs a slow course, is never recovered from spontaneously, and, unless removed, terminates after many years in death from exhaustion.

History and geographical distribution.—The earliest notice of this disease we owe to Kæmpfer (1712). Its more modern history commenced with Godfrey, of Madras, who, in the *Lancet* of June 10th, 1843, gave a description of several unquestionable examples under the title, "Tubercular Disease of the Foot." Subsequently Balingall (1855), who was the first to suggest its parasitic nature, Eyre (1860), and others added considerably to our knowledge of the subject. The merit of bringing the disease prominently before the profession, and of distinctly describing its clinical and anatomical features, as well as of suggesting its true pathology, belongs entirely to Vandyke Carter, who, from 1860 to 1874, in a series of important papers, furnished the information on which all later descriptions have been principally founded. Carter was the first to point out the presence of mycotic elements in the discharges coming from the implicated structures, and in the contents of the characteristic cysts and sinuses with which they are honeycombed, and showed that the disease was allied to actinomycosis. Recently much information has been supplied by Wright, Nicolle, Laveran, Bauffard and, especially, by Brumpt (*Arch. du Parasitologie*, Trans. X., 1906).

In India mycetoma is endemic in districts more or

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less limited. These districts are scattered over a wide area, the intervening regions—in some instances whole provinces, as that of Lower Bengal—enjoying an almost complete immunity. It appears to be acquired only in rural districts, the inhabitants of the towns being exempt. Among the most afflicted districts may be mentioned Madura—hence the name "Madura foot" by which mycetoma is often known—Hirsar, Ajmeer, Delhi, various places in the Punjab, Kashmir, and Rajputana. In recent years we have accounts of its occurrence with some degree of frequency in Senegambia, Somaliland, Algeria, Egypt, the Soudan, Cochin China, Italy, the United States, and in South America. It is probable that in time mycetoma will be found to be endemic in many warm countries in which it has hitherto escaped recognition.

Symptoms.—Mycetoma begins usually, though by no means invariably, on the sole of the foot. The first indication of disease is the slow formation of a small, firm, rounded, somewhat hemispherical, slightly discoloured, painless swelling, perhaps about half an inch in diameter (Fig. 157). After a month or more this swelling may soften and rupture, discharging a peculiar viscid, syrupy, oily, slightly purulent, sometimes blood-streaked fluid containing in suspension certain minute, rounded, greyish or yellowish particles, often compared to grains of fish roe. In other examples of the disease the particles in the discharge are black, having the size and appearance of grains of coarse gunpowder. Sometimes these particles are aggregated into larger masses up to the size of a pea. In time additional swellings, some of which break down and form similar sinuses, appear in the neighbourhood of the first or elsewhere about the foot. For the most part the sinuses are permanent, healing up in a very few instances only. Gradually the bulk of the foot increases to perhaps two or three times the normal volume (Fig. 158). There is comparatively little lengthening of the foot; but there is a general increase in thickness, so that in time the mass comes to assume an ovoid form, the sole of the

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Fig. 157.—Mycetoma of about two years' standing. (*After Legrain.*)

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member becoming convex, the sides rounded, and the anatomical points obliterated. The toes may be forced apart, bent upwards at the tarso-phalangeal joints, or otherwise misdirected; so that on the foot being placed on the ground the toes do not touch it. The surface of the skin is roughened by a number of larger or smaller, firmer or softer hemispherical elevations, in some of which the orifices of the numerous sinuses open. Most of these orifices are easily made out; others are not so apparent, their position

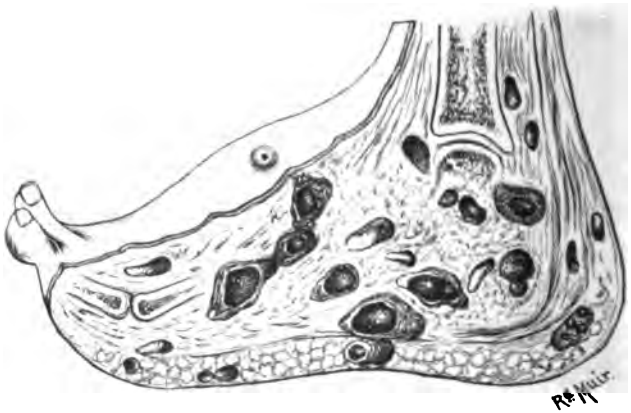

Fig. 158.—Section of a Madura foot. (*T. R. Lewis.*)

being indicated and, at the same time, concealed by a bunch of pale, flabby, fungating, and but slightly vascular granulations. In the latter the orifice may be hard to find. Once the probe is got to enter, the instrument readily passes to a considerable depth, even to the bone; in advanced cases it can be carried through the softened tissues with the greatest ease in almost any direction, and without causing much pain or hæmorrhage.

The discharge issuing from the sinuses differs in amount in different cases, and from time to time in the same case; whether profuse or scanty, it always exhibits the same oily, mucoid, slightly purulent

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appearance, and may stink abominably. With a very few exceptions it contains either the grey or the black grains already referred to; rarely similar bodies of a reddish or pink colour.

To the touch the swollen foot feels somewhat elastic, and does not readily pit on pressure. The sensibility of the skin is preserved. Although complained of in some instances, severe pain is rarely a prominent feature. The principal complaint is of inconvenience from the bulk and weight of the mass, and, in advanced cases, of the uselessness of the limb for locomotion. In time the foot is no longer put to the ground, different unnatural styles of progression being adopted by different patients.

As the foot enlarges the leg atrophies from disuse; so that in the advanced disease an enormously enlarged and misshapen foot, flexed or extended, is attached to an attenuated leg consisting of little more than skin and bone. In some the tibia, or the bones of the forearm, as the case may be, become involved; in others the disease at first may be confined to a toe, or a finger, or other limited area. In a very few instances the seat of the disease is the knee, thigh, jaw, or neck. Unless the case be one of actinomycosis, the internal organs are never specifically implicated, either primarily or secondarily. The lymphatic glands likewise, although they may be the subject of adenitis from secondary septic infection, are very rarely involved.

After ten or twenty years the patient dies, worn out by the continued drain, or carried off more suddenly by diarrhœa or other intercurrent disease.

Classification, ætiology, and histology.—Formerly the tropical forms of mycetoma were classified according to the colour of the mycotic particles in the discharge. Thus we had the white or ochroid, the black or melanoid, and the red forms of mycetoma, the last being a very rare variety. Brumpt's investigations have made a classification more scientific than this crude clinical one possible; the latter, therefore, has to be abandoned.

This authority distinguishes eight different kinds

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of mycetoma, two of which are caused by species of *Discomyces*. Of the other six, two are certainly caused by species of *Aspergillus*. The remaining four are also probably due to species of Aspergillus; but, in the absence of cultural evidence, he places them in two provisional groups, one of which, embracing the unpigmented septate species, he names *Indiella*, the other, the pigmented species, he calls *Madurella*. Moreover, he has shown that the fungi which give rise to mycetoma may present not only resisting forms such as *sclerotia* and *chlamydospores*, but also characteristic spore apparatus (*Aspergillus nidulans*, *A. bouffardi*). The species are as follows:

I.—ACTINOMYCOTIC MYCETOMA.

Caused by the ray-fungus, *Discomyces bovis* (Harz, 1877). Actinomycosis has a world-wide distribution and is a common disease of cattle. It occurs also in hogs. In men it may attack the extremities, giving rise to a tumour clinically undistinguishable from other kinds of mycetoma, or it may develop in the jaw, the tongue, lungs, liver, brain, and occasionally the primary lesion may be followed by metastases in all parts of the body.

The fungus of actinomycosis develops equally well in most tissues. It destroys bone by erosion and spares only nerves and tendons. The pus from the affected region contains small yellowish granules ("sulphur grains") of irregular shape, attaining at most 0·75 mm. in diameter. They are soft and consist of an inextricable felted mass of mycelia. The threads are radially arranged at the periphery of the grain, and their free extremity widens into a bulbous, club-like termination (10–20 μ long by 8–10 μ wide). These clubbed ends have been looked upon by several authors as forms of degeneration Brumpt points out that they consist of young, active protoplasm, and holds that they are functionally hypertrophied while elaborating food for the colony. In old grains the clubs disappear, their protoplasm being utilised in the formation of spores.

This fungus gives rise to ramified sinuses which extend in all directions, opening at the surface by numerous vents. The sinuses are surrounded by a thick fibrous sheath of connective tissue. The centre of the largest tunnels is softened, the youngest grains being at the periphery surrounded by polynuclear cells and almost in contact with the sclerosed tissues which separate the cavities and sinuses.

The parasite has been successfully cultivated and the disease has been inoculated both with the natural and the artificially grown organism.

Discomyces bovis lives saprophytically on certain plants. It

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has been found on the spikelets of cereals (*Hordeum murinum* L., *Phleum pratense* L., etc.), and is therefore probably inoculated through the skin or mucous membranes in the same way as the fungi which give rise to other kinds of mycetoma.

The diagnosis of the disease from tertiary syphilis and bone tuberculosis rests on the characteristic grains present in the pus.

The disease is progressive and of grave import. The treatment is largely surgical. In early cases iodide of potassium in doses of from 40 to 60 grains daily has proved advantageous and in some cases even curative.

II.—VINCENT'S WHITE MYCETOMA.

Caused by *Discomyces maduræ* (Vincent, 1894). This kind of mycetoma is common and widely distributed. It has been observed in Algeria, in Abyssinia, in Somaliland, in the island of Cyprus, in India, in the Argentine Republic, and in Cuba.

It runs a slow course. Unlike *D. bovis* and other mycetoma-producing fungi, it does not destroy bone, and does not seem to act directly on the general health of the patient, though ultimately and indirectly it may bring about cachexia.

The grains formed by *Discomyces maduræ* vary in size from that of a pin's head to that of a pea. They are of a yellowish-white colour, present a mulberry-like surface, are soft and easily crushed. Their mode of growth is absolutely characteristic. The grain throws out from its periphery radiating filaments. Between these fungus threads are numerous lymphocytes (likewise arranged in radial series) embedded in an amorphous substance, probably arising from the destruction of lymphocytes, epithelial cells, and macrophages, on which the mycelium feeds. The crown of amorphous rays round the grain is typical. The grain is surrounded by numerous polynuclear leucocytes. Having attained from 1 to 1·5 mm. diameter, the grain projects small shoots which become detached from the parent grain, enlarge and reproduce the characteristic radial structure. Other grains form also, and, after a time, the typical large mulberry granule is formed, the central grains degenerating. The grains are found in cavities surrounded by inflammatory connective tissue permeated by polynuclear cells and occasionally giant cells.

III.—NICOLLE'S WHITE MYCETOMA.

Caused by *Aspergillus nidulans* (Eidam, 1883). So far only one case has been observed in Tunis, but probably it occurs in many places, the parasite, *Aspergillus nidulans*, being widely distributed. The grains formed by this fungus may also attain the size of a pea, but they differ from those of *Discomyces maduræ*, inasmuch as they are more or less spherical and present a smooth surface.

In this form of mycetoma the bones are attacked and destroyed.

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IV.—BOUFFARD'S BLACK MYCETOMA.

Caused by *Aspergillus bouffardi* (Brumpt, 1906). This form was discovered by Bouffard at Djibouti, Somaliland. Lewis seems to have met a similar case in India; a third case, probably also belonging to this species, was described by Bovo in Italy.

The grains are quite characteristic. They are black in colour and vary in size from a pin's head to that of No. 1 shot. They present a mulberry-like surface which is smooth and glossy. They are somewhat elastic, but break when pressed. Their structure is remarkable. It consists of a coiled-up mass. Maceration in water for about 24 hours causes the grain to unfold. Sections show that the grain is composed of a densely felted mycelium of a silvery-white colour, with a peripheral zone of irregularly moniliform threads with terminal chlamydospores cemented together by a dark brown interstitial substance.

The grains are found in the cellular tissue, always singly and within small cavities. Each grain is surrounded by enormous giant cells, and by epithelioid cells of all sizes, and is enclosed in a characteristic shell of connective tissue.

This kind of mycetoma appears to be more amenable to treatment. Bouffard's and Bovo's cases were radically cured by curettage. In Bovo's case a secondary extension to the groin lymphatics of the affected side had suggested the diagnosis of melano-sarcoma.

V.—CLASSIC BLACK MYCETOMA.

Caused by *Madurella mycetomi* (Laveran, 1902). This mycetoma has a very wide distribution. It has been observed in Italy, in Africa (Senegal, French Soudan), and in India.

The grain formed by *Madurella mycetomi* is dark brown or black in colour. It measures 1 to 2 mm. in diameter, is hard and brittle; its surface is irregular and frequently presents pointed eminences which differentiate it from the larger and smooth grains of *Aspergillus bouffardi*. The grain is composed of white threads, always over 1 μ in diameter and attaining at times 8 to 10 μ, which secrete a dark brown substance that cements them together. The grain is first surrounded by giant cells, epithelioid cells, and numerous polynuclear cells, and shows numerous chlamydospores at the periphery. Then a thick capsule of fibrous connective tissue forms round it. This puts an end to the vegetation of the fungus, which passes into a resting stage and is converted into sclerotia, in which form it is eliminated. This was shown by Carter as early as 1860. The grains form rapidly within the tissues. Brumpt reports a case in which they were eliminated in large numbers one month after the commencement of the disease.

Each grain may become the centre of an active colony, which continues to extend, destroying the surrounding tissues, until arrested by a barrier of sclerosed tissue. Thus large

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tumours may be formed. In very old grains the mycelium presents cavities filled with numerous chlamydospores. Sometimes, on account of unfavourable conditions, certain lobes of the fungus separate from the rest of the colony and become independent grains. This mode of vegetation, characteristic of the species, gives to the lesions a typical rosette-like appearance.

VI.—Brumpt's White Mycetoma.

Caused by *Indiella mansoni* (Brumpt, 1906). This form was described from a specimen of Indian origin in the Museum of the London School of Tropical Medicine.

The grains peculiar to this form are hard, white, and very small, varying in size between $\frac{1}{3}$ and $\frac{1}{4}$ of a millimetre and having a lenticular shape. Some are bean-shaped and flat. To study their structure it is necessary to boil them first in a solution of caustic potash. The hyphal threads are large and closely set, but without any cementing substance between them. The periphery of the grain contains numerous large chlamydospores with thick wall and full of protoplasm.

The grains of *Indiella mansoni* are always numerous within the inflammatory tissue. The latter is brownish and is not surrounded by a well-marked sheath of connective tissue as in other mycetomas. It contains numerous polynuclear cells, a few lymphocytes and some macrophages.

VII.—Reynier's White Mycetoma.

Caused by *Indiella reynieri*, Brumpt, 1906. This form was found in Paris by Reynier.

The grains may attain 1 mm. in diameter; they are soft white and consist of a coiled-up strand, which gives them a peculiar appearance resembling the excrements of earthworms. They are made up of a dense felting of hyphal threads, the peripheral branches of which usually terminate in chlamydospores divided into two or three compartments. The hyphæ are bound by a scanty cement, which is easily dissolved out by boiling in caustic potash.

VIII.—Bouffard's White Mycetoma.

Caused by *Indiella somaliensis*, Brumpt, 1906. This form is perhaps even more common in India than Vincent's white mycetoma. Bouffard has found it twice in Somaliland.

Indiella somaliensis is a most destructive fungus. In a foot examined by Brumpt all the muscles, tendons and bones had been replaced by sclerosed tissues more or less homogeneous and presenting numerous sinuses full of yellowish grains clustered together like fish-roe, and many small inflammatory nodules containing one or more grains.

The grains vary in colour from white to reddish yellow; they are small, smooth, and attain on an average about 1 mm. in diameter. They are spherical when single, but polyhedric from reciprocal pressure when clustered in masses. The parasite in its earliest stage is always found in a giant

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cell, showing as an irregular mass which stains more deeply than the enclosing cell. Usually several infected cells coalesce; the grain which results is surrounded by an amorphous layer produced by the destruction of the elements which form its substratum. The grains are not enclosed within nodules, as is the rule in certain mycetomas, but spread exactly like those of actinomycosis.

In the amorphous zone of cellular detritus Brumpt found a discomyces which seems to live symbiotially with *Indiella somaliensis*. In attempts at culture Bouffard found that this discomyces was the only organism that grew.

Morbid anatomy.—On cutting into a mycetomatous foot or hand the knife passes readily through the mass, exposing a section with an oily, greasy surface, in which the anatomical elements in many places are unrecognisable, being, as it were, fused together, forming a pale, greyish-yellow mass. The bones in parts have entirely disappeared; where their remains can still be made out the cancellated structure is very friable, thinned, opened out, and infiltrated with oleaginous material. Of all the structures the tendons and fasciæ seem to be the most resistant.

The most remarkable feature revealed by section is a network of sinuses and communicating cyst-like cavities of various dimensions, from a mere speck to a cavity an inch or more in diameter. Sinuses and cysts are occupied by a material unlike anything else in human morbid anatomy. In the black varieties of mycetoma this material consists of a black or dark brown, firm, friable substance which, in many places, stuffs the sinuses and cysts; manifestly it is from this that the black particles in the discharge are derived. In the white varieties the sinuses and cysts are also more or less stuffed with a white or yellowish roe-like substance, evidently an aggregation of particles identical with those escaping in the corresponding discharge. The black substance, which can be readily turned out, is moulded into truffle-like masses ranging in size from a mere grain to a small apple, according to the capacity of the cysts or sinuses containing it. The roe-like particles in the white varieties are held together by a softer cheesy-looking material. The sinuses and cysts occupy the

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bones, muscles, or fasciæ indiscriminately; they are found principally in the fat and connective tissue. They are lined with a smooth membrane, adherent when in the soft tissues, but capable of being enucleated when in the bones. Some of the cysts do not communicate with sinuses; most of them, however, do so and with each other, opening on the surface of the skin at the mamillated fistulæ already referred to. In the very rare red variety the colour of the accretions is red or pink.

Under the microscope the mycotic elements can be readily recognised in the concretions. In microscopical sections of the tissues evidences of extensive degenerative changes, the result of a chronic inflammatory process, can be made out. An important feature as bearing on the pathology of the disease, and one which was long ago described by Lewis and Cunningham, has been insisted on more recently by Cunningham, namely, a sort of arteritis obliterans or extensive proliferation of the endothelium of the arteries and, according to Vincent, a thickening of the adventitia of the vessels as well as of the capillaries in the more affected areas.

Mode of entrance of the fungus.—Little is known on this point. It is conjectured that the fungi live as parasites on certain plants, and that they may penetrate the tissues of man through a wound in the skin. The peculiar endemicity and geographical distribution of the disease, and the facts of its occurring almost invariably on the feet or hands, and principally in bare-footed agriculturists, favour this view.

Treatment.—The only effective treatment, in the case of implication of a considerable part of the foot or hand, is amputation. This must be performed well above the seat of the disease; for it must be borne in mind that the long bones may be implicated as well as the small bones, and that unless the entire disease be removed it will recur in the stump. Complete removal is not followed by relapse. If a toe, or a small portion of the foot or hand, is alone involved, this may be excised with success. Potassium iodide has been found to be beneficial in certain forms.

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DHOBIE'S ITCH.

In view of the recent researches of Sabouraud and others on the ringworms of Europe, there can be little doubt that the ringworms of warm countries are attributable to a large variety of fungus forms, probably many of them derived from the lower animals. Although, in a general way, we are familiar enough with the clinical features of these ringworms, their specific germs have not as yet been very closely studied. By the lay public all epiphytic skin diseases, more especially all forms of intertrigo, are spoken of as dhobie's (washerman's) itch, in the belief, probably not very well founded, that they are contracted from clothes which have been contaminated by the washerman. There are many sources of ringworm infection in warm climates besides the much maligned dhobie.

In the tropics, native children often exhibit dry, scurfy patches of ringworm on the scalp; and the skin of the trunk and limbs of adults is not unfrequently affected with red, slightly raised, itching rings, or segments of rings, of trichophyton infection. Sometimes these rings enclose areas many inches in diameter.

Pityriasis versicolor is also very common in the tropics. It is the usual cause of the pale, fawn-coloured, slightly scurfy patches so frequently a feature on the dark-skinned bodies of natives. On the dark-pigmented skins of negroes, Indians, and dark-complexioned Chinese, the patch of pityriasis—contrary to what obtains in Europeans and light-skinned Chinese—is usually paler than the healthy integument surrounding it. The pigment in the fungus and the profuse growth of the latter conceal, as a coat of paint might, the dark underlying natural pigment of the skin, which, moreover, in certain cases, seems to be affected (either increased or decreased) by the action of the fungus. Castellani has recently studied the several forms of mycotic pityriasis as they occur in Ceylon. He recognises three forms: *Pityriasis versicolor flava*, produced by *Microsporon tropicum*, a fungus having a thick

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irregular constricted mycelium; *Pityriasis versicolor alba*, produced by a very minute fungus with straight, short mycelia—*Microsporon macfadyeni*; and *Pityriasis versicolor nigra*—a variety I had described many years ago as occurring in South China—produced by *Microsporon mansoni*, which contains much dark pigment in the mycelial tubes, and which on culture in maltose agar produces black hemispherical colonies.

The expression *dhobie's itch*, although applied to any itching, ringworm-like affection of any part of the skin, most commonly refers to some form of epiphytic disease of the crutch or axilla. There are at least three species of vegetable, or bacterial parasites which in the tropics are prone to attack these situations—namely, the trichophytons or ordinary body ringworms, the *Microsporon minutissimum* of erythrasma, and the germ of the disease I have described under the name pemphigus contagiosus.

The suffering which some of the forms of dhobie's itch give rise to is often severe. In hot, damp weather especially, the germs proliferate actively, producing, it may be, smart dermatitis. The excessive irritation leads to scratching and, very likely, from secondary bacterial invasion, to boils or small abscesses. The crutch, or axillæ, or both are sometimes rendered so raw and tender that the patient may be unable to walk or even to dress. The irritation and itching are usually worse at night, and may keep the patient awake for hours. Even in the absence of treatment, when the cold season comes round the dermatitis and irritation subside spontaneously. The affected parts then become dry, pigmented, and scurfy, and the fungus remains quiescent until the return of the next hot weather.

Diagnosis.—The diagnosis of mycotic dermatitis is usually easily made. The festooned margin is almost conclusive. In the case of pemphigus contagiosus the characteristic blebs, the smooth, raw, or glazed surfaces and undermined epidermic rings are usually very apparent and render diagnosis easy. When doubt exists, recourse to the microscope may

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be necessary; but, owing to the inflamed condition of the parts, there may be much difficulty in finding fungus elements even when the case is certainly epiphytic. A negative result is, therefore, not always conclusive against ringworm.

I am convinced that many cases of dhobie's itch are produced by *Microsporon minutissimum*, and that they are really inflamed erythrasma and not trichophyton ringworm. During cold weather one often sees on the site of what, during the summer, had been a troublesome dhobie's itch, a brownish furfuraceous discoloration of the crutch or axilla. The same appearance I have remarked in Europe in Europeans who had suffered from dhobie's itch in the East, and on examining scrapings from the parts have found *M. minutissimum* in abundance. It would seem, therefore, that during the heat and moisture of a tropical summer this generally very unirritating parasite becomes more active and excites dermatitis. The same may sometimes be seen in pityriasis versicolor. I believe that those cases of *Microsporon—furfur* and *minutissimum*—dhobie's itch are more easily cured than the trichophyton varieties.

Treatment.—After a thorough use of soap and water, the application of Vleminck's solution of sulphuret of calcium (1 oz. quicklime, 2 oz. precipitated sulphur, 15 oz. water, boiled together in an earthenware vessel till reduced to 10 oz.; decant the clear sherry-coloured fluid after subsidence) every night for three or four times generally brings about a rapid cure. If the parts are inflamed and tender the solution should be diluted to half or one quarter strength for the first two applications. A tincture of the leaves of *Cassia alata* painted on, or the crushed leaves themselves well rubbed in, are equally successful. If these fail, chrysophanic acid ointment, twenty grains to the ounce of vaseline, rubbed in twice a day till a slight erythema shows at the edge of the diseased patch, is almost invariably successful. When prescribing chrysophanic acid the physician must be careful to inform the patient of its staining effect on clothes; to warn him to stop its use so soon as the

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erythematous ring shows; and to be careful not to apply the ointment to the face. A writer in the *Indian Med. Gaz.* (Jan., 1898) strongly recommends the application of glacial acetic acid. It cures, he affirms, with, at most, two applications. The smarting its use entails is relieved by laying a lump of ice in a handkerchief on the part. For the ringworms of the thick-skinned natives linimentum iodi freely applied, and of double strength, is the best, and a most efficient remedy.

Prophylaxis.—The various forms of crutch dhobie's itch may be avoided by wearing next the skin short cotton bathing-drawers and changing them daily; at the same time powdering, after the daily bath, the axillæ and crutch with equal parts of boric acid, oxide of zinc, and starch.

TINEA IMBRICATA (Plate VII.).

Definition.—A form of body ringworm, until lately peculiar to certain Eastern oceanic tropical climates, produced by a trichophyton (lepidophyton, Tribondeau), and characterised by a concentric arrangement of closely set rings of scaling epidermis.

Geographical distribution.—This peculiar form of epiphytic disease is strictly confined to warm climates. It is principally met with in the Eastern Archipelago and in the islands of the South Pacific, although it has been found to extend westward as far as Burma, and northward as far as Foochow and Formosa on the coast of China. In many of the islands of the South Pacific it affects a large proportion of the inhabitants; in some islands quite one-half. There is good reason to believe that its area of distribution is gradually extending. Thus Turner and Königer tell us that it was formerly unknown in Samoa and Bowditch Islands, where it is now very prevalent. Daniels informs me that it was introduced for the first time into Fiji by some Solomon Islanders in 1870; by 1872 it had become general among the Fijians. It was recently introduced into Tahiti, and rapidly spread there among the

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natives. We have no accounts of such a disease in Africa. Recently it has been described by Paranhos and Leme as occurring in the interior of Brazil. Once introduced, it spreads very rapidly in countries with a damp, equable climate and a temperature of 80° to 90° Fahr. Very high or very low temperatures and a dry atmosphere are inimical to its extension.

Symptoms.—Tinea imbricata is easily recognised. At first it may be confined to one or two spots on the surface of the body; usually, in a short time, it comes to occupy a very large area. It does not generally affect the soles and palms, although it may do so; nor is the scalp a favourite site. Baker, confirmed by Tribondeau, remarks that it avoids the crutch, the axillæ, and the nails. With these exceptions it may, and commonly does, sweep over and keep its hold on nearly the entire surface of the body; so that after a year or two a large part of the skin is covered with the dry, tissue-paper-like scales, arranged in more or less confused systems of concentric parallel lines, absolutely characteristic of the disease.

An inoculation experiment readily explains the production of the scales, their concentric parallel arrangement, and the mode of extension of the patches. About ten days after the successful inoculation of a healthy skin with tinea imbricata, the epidermis at the seat of inoculation is seen to be very slightly raised and to have a brownish tinge. Presently the centre of this brownish patch—perhaps a quarter of an inch in diameter—gives way and a ring of scaling epidermis, attached at the periphery but free, ragged, and slightly elevated towards the centre of the spot, is formed. In a few days this ring of epidermis has extended so as to include a larger area. A second brown spot then appears at the site of the first brown spot and in the centre of the primary scaling, expanding ring. This second spot, in its turn, gives way, producing a second and similar scaling ring, which also expands, following the first ring in its extension. Later a third and fourth ring form in the same way; and so on, until a large area of skin is covered with one or

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PLATE VII.—Tinea Imbricata.

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more systems of concentric parallel scaling rings, which follow each other over the surface of the body like the concentric ripples produced by a stone falling into a pool of water.

The scales, if not broken by rubbing, may attain considerable length and breadth; but, of course, their dimensions are in a measure determined by the amount of friction they are subjected to. Usually they are largest between the shoulders—that is, where the patient has a difficulty in scratching himself. The lines of scales are from one-eighth of an inch to half an inch apart. The hair of the scalp is not injured.

The fungus.—On detaching a scale and placing it under the microscope, after moistening with liquor potassæ, a trichophyton-like fungus can be seen in enormous profusion. This fungus has not been cultivated, but Tribondeau, on the evidence of finding fructification in one observation, pronounces it to be a lepidophyton and not a trichophyton. The parasite evidently lies between epidermis and rete, and by its abundance causes the former to peel up. As the fungus does not die out in the skin travelled over, it burrows under the young epithelium almost as soon as the latter is reproduced. Hence the peculiar concentric scaling and the persistency of the disease throughout the area involved. When the scales are washed off by the vigorous use of soft soap and hot water, the surface of the skin is seen to be covered with parallel lines of a brownish colour—evidently the slightly pigmented fungus proliferating and advancing under the young epidermis.

Diagnosis.—From ordinary ringworm tinea imbricata is easily distinguished by the absence of marked inflammation or congestion of the rings, by the abundance of the fungus, by the large size of the scales, by the concentric arrangement of the many rings or systems of rings, by the non-implication of the hair, and, according to Baker, by the avoidance of crutch and axillæ. From ichthyosis it is distinguished by the concentric arrangement of the scaling, by the peripheral attachment of the scales, and by the presence of abundant fungus elements.

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Treatment.—The best treatment for tinea imbricata in natives is the free application of strong linimentum iodi. Limited patches might be treated with chrysophanic acid ointment (twenty grains to one ounce) or by the inrubbing of bruised *Cassia alata* leaves. Paranhos and Leme recommend the following:—A tepid alkaline bath of sodium bicarbonate (1 kilogramme to 20 litres of water), followed by the application of the following—Ocalia perdiceps, 50 grammes; glacial acetic acid, 15 grammes; macerated for two days in glycerinated water (10 per cent.) 985 grammes, and then filtered. Sulphur ointment, or sulphur fumes, act very slowly and unsatisfactorily. Clothes should be boiled or burned.

Prophylaxis.—Daniels informs me that tinea imbricata is comparatively rare in Tonga. This circumstance the natives attribute to their custom of oiling the body. Daniels remarks that of late years, since the Fijians adopted the same practice, the disease has become somewhat less prevalent among them. Cleanliness, and the immediate and active treatment of any scaling spot, should be carefully practised in the endemic countries.

In Tahiti the use of chrysophanic acid is now general among the natives; as a consequence the disease is not so prevalent there as it was only a few years ago.

PINTA.

Definition.—An epiphytic disease characterised by peculiar pigmented patches on the skin.

Geographical distribution.—In certain districts in tropical America, especially along the river banks in Mexico, Central America, Venezuela, Colombia, Bolivia, and one or two places in Peru, Chili, and Brazil—the district between the Juciparana and the Santo Antonio rivers (Magalhães, private letter)—there occurs an epiphytic skin disease characterised by peculiar red, or blue, or black, or white piebald spotting of the skin of a part, or of the whole, of the body. The patient emits an offensive odour, sometimes compared to that of a mangy dog, or of dirty

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linen. Desquamation and itching of the patches are also features of the disease. It entails no constitutional disturbance and no danger to life. Like other epiphytic diseases, want of personal cleanliness has a great deal to do with the prevalence of pinta in the districts mentioned, for it is rare in cleanly whites or well-to-do negroes; the dirty Indians and the poor half-castes are those most frequently affected. In some districts it occurs in nearly a tenth part of the inhabitants, in others nearly the entire population is affected. Lately a somewhat similar disease has been seen in North Africa,* in Egypt, and possibly in the Malay peninsula.

Symptoms.—Pinta commences at one or two points, the rest of the surface becoming infected in turn by extension or by auto-contagion. At first the hands, or face, or some other exposed parts, are attacked. The original patch may be white, red, blue, or black. It gradually increases in size, becoming scurfy and itchy, particularly when the surface is warm. As the patches spread they assume a variety of shapes. Fresh spots appear in the neighbourhood of the parent spots, into which, in course of time, they tend to merge; so that ultimately large patches of discoloured skin are formed. The palms of the hands and the soles of the feet are not attacked. On the scalp becoming affected the hair turns white and thin, and ultimately falls out. When fully developed, the disease produces a very grotesque appearance. It is probable that the white patches in a proportion of

* It is difficult from his description to determine the exact nature of the disease alluded to by Legrain. It commences with pronounced fever lasting for one week, and is followed by malaise persisting for several weeks. This is followed by itching and, by-and-by, by furfuraceous desquamation of the itching parts and gradually developed achromia. He positively affirms that the disease is not ordinary vitiligo. He also says he has seen in Tripoli a coloured skin affection with the clinical features of true pinta occurring in little epidemics in particular houses. The results of microscopical examinations of scrapings of the affected skin were negative. Possibly this is the disease referred to in the *Journ. of Trop. Med.*, Nov., 1899, by Sandwith, as having been seen by him in Egypt. Varieties of pityriasis versicolor, such as Castellani has described in Ceylon, may have been mistaken sometimes for true pinta.

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cases are not epiphytic, as they neither itch nor desquamate; very likely they are ordinary leucodermia, possibly brought about by disturbance of the natural pigmentation by a parasite which had subsequently died out. Sensation and the glandular functions of the skin are not affected. In consequence of the scratching, the implicated parts may become cracked or ulcerated.

Two types of the disease have been named—the superficial epidermic and the deep epidermic; the former being represented by black and blue patches which spread rapidly; the latter including the red and white patches, apparently involving the rete and deeper layers of the epidermis, spreading more slowly, and, at the same time, being more difficult to cure. The various forms and colours may concur in the same individual; but a given patch, once established, does not change colour.

Pinta is contagious. It attacks both sexes and any age. Unless properly treated it may last for years.

Pathology.—If one of the scales is moistened with liquor potassæ and placed under the microscope, black spores and a white, highly refracting mycelium are found. The spores are round or oval, measuring 8 μ to 12 μ in diameter. Abundant pigment is seen floating in a yellowish fluid in the interior of the spore. The mycelial filaments are short, non-branching, tapering from a broad base to a blunt point by which each filament is attached to a single spore, like the stalk to a cherry. The mycelium measures from 18 μ to 20 μ in length by 2 μ in breadth. The differences in the colour of the patches probably depend on differences in the pigmentation, or kind, of the fungus. Such is Gastambide's description of the parasite, a description which, to some extent, is borne out by Osborne Browne.

Montoya y Florez has published an elaborate and careful description of the disease and of the various mycotic growths he found in the several varieties of pinta which he studied. He says that he has never seen a fungus answering to Gastambide's description. On placing the scales

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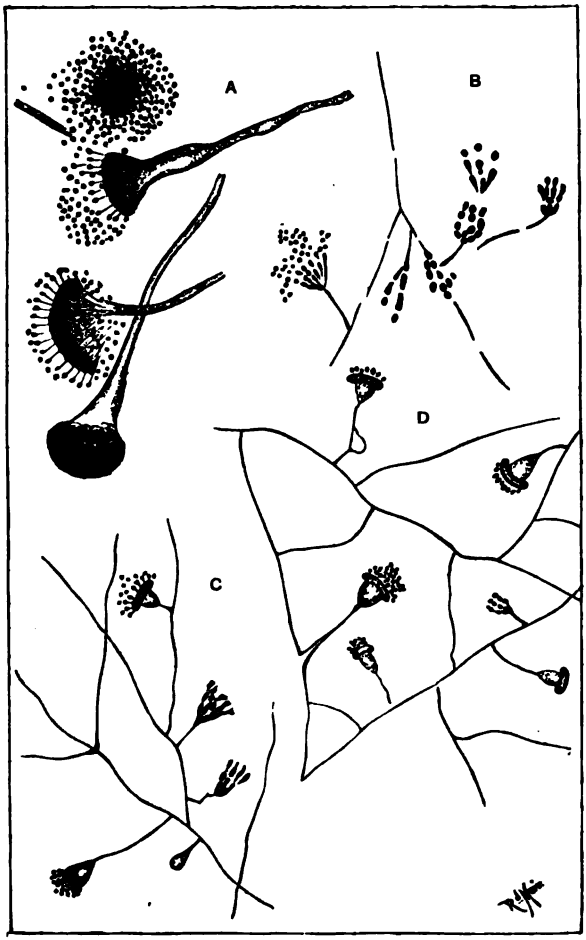

Fig. 159.—Fructification of cryptogamic epiphytes in pinta.
(*After Montoya y Florez.*)

A, red pinta; B, dark violet pinta; C, grey violet pinta; D, blue pinta.

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moistened with liquor potassæ under the microscope, long, dichotomous filaments, generally very fine and cylindrical, in certain conditions granular and beaded, are seen. In places this mycelium forms a dense network. Here and there veritable ropes of mycelium are visible, or broad, short filaments with fructification characteristic of the particular variety of the disease may be detected (Fig. 159). He has succeeded in cultivating the various fungi, which apparently belong to a plurality of genera — *Penicillium*, *Aspergillus*, *Monilia*.

Diagnosis.—This disease is readily diagnosed from leprosy by the absence of anæsthesia in the patches, and by the colour of the spots; from erythrasma, from ringworm, and from pityriasis versicolor by the colour, and by the microscopical characters of the fungus.

Treatment.—Chrysophanic acid, preparations of sulphur, strong liniment of iodine, and other epiphyticides are indicated. Cleanliness and the destruction of old clothes are indispensable.

PIEDRA.

This peculiar disease of the hair is very common in certain districts of Colombia, South America. So far as is known, it is confined to the inhabitants of that country, of whom a considerable proportion, both male and female, and apparently belonging to all the races represented there, are affected.

According to Juhel-Rénoy, whose observations practically coincide with the earlier accounts by Desenne, Cheadle, Morris and others, the hairs of the affected scalp are dotted over at irregular intervals with numerous—twenty-three in a hair sixty centimetres in length—minute, gritty nodosities. These, barely visible to the naked eye, are distinctly perceptible to the touch when the hair is drawn between finger and thumb. The affected hairs are bent and twisted, and tend to produce matting and knotting. The little nodosities, which, though very firm, are not so hard as the name piedra (a stone) would indicate, being easily cut through with a sharp knife or scissors, are paler

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than the hair which they surround, or partly surround, like a sheath. When a comb is drawn through the hair a sort of crepitation is produced, doubtless by the friction against the hard particles.

Under the microscope these excrescences are found to consist of a number of spore-like bodies, easily made apparent by soaking the hair in liquor potassæ after washing in ether. The spores (which are twice the size of trichophyton spores and remarkably refringent) from mutual pressure are polyhedral, and together form a sort of tesselated mosaic, the elements of which seem to be held together by a greenish soluble cement in which a number of minute bacteria-like rods are incorporated. The shaft of the hair is not eroded or affected in any way; it can be seen intact through the encrusting fungus.

Piedra is supposed by some to be induced by the mucilaginous hair applications in vogue among the Colombians. Although Juhel-Rénoy has given to it the name "trichomycose nodulaire," it must not be confounded with the trichomycosis nodosa of Paterson (the leptothrix of Wilson), which is quite a different affection and common enough on the axillary, scrotal, and face hair in Europe and elsewhere. Neither must it be confounded with trichorexis nodosa, a non-parasitic disease of the hair-shaft, which is split up at different points into brush-like bundles of fibres and is thus easily fractured; nor with moniliform hair (monilethrix, Crocker), a congenital, hereditary, and also non-parasitic disease.

Treatment.—Cleanliness, the free use of soap, and the application of some epiphyticide should suffice for cure. Should such means fail, doubtless shaving the scalp would be effectual.

IV.—Caused by Animals.

The Chigger or Sand Flea (*Dermatophilus penetrans*).

This insect, formerly confined to the tropical parts of America (30° N. to 30° S.) and to the West Indies, appeared on the West Coast of Africa for the first time about the year 1872. Since that date it has spread all over the tropical parts of that continent

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and even to some of the adjacent islands—Madagascar for example. As a cause of suffering, invaliding, and indirectly of death, it is an insect of some importance. It is now extremely prevalent on the East Coast of Africa, and is causing a large amount of invaliding amongst the Indian coolies there, by whom it has been introduced into India.

Fig. 160.—Chigger (Dermatophilus penetrans). (*Blanchard.*)

The chigger (Fig. 160) is not unlike the common flea (*Pulex irritans*) both in appearance and, with one exception, in habit. It is somewhat smaller in size—1 mm., the head being proportionately larger and the abdomen deeper than in the

Fig. 161.—Chigger: impregnated female. (*Blanchard.*)

latter insect. In colour it is red or reddish brown. Like the flea, its favourite haunt is dry, sandy soil, the dust and ashes in badly kept native huts, the stables of cattle, poultry pens, and the like. It greedily attacks all warm-blooded animals, including birds and man. Until impregnated, the female, like the male, is free, feeding intermittently as opportunity offers. So soon as she becomes impregnated she avails herself of the first animal she encounters to burrow diagonally into its skin, where, being well nourished by the blood, she proceeds to ovulation. By the end of this process her abdomen, in conse-

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quence of the growth of the eggs it contains, has attained the size of a small pea (Fig. 161). The first anterior and the two posterior segments do not participate in the enlargement, the latter acting as a plug to the little hole made by the animal when she entered the skin. When the ova are mature they are expelled and fall on the ground. In a short time a thirteen-ringed larva is hatched out from each egg. This larva presently encloses itself in a cocoon, from which, in eight or ten days, the perfect insect emerges.

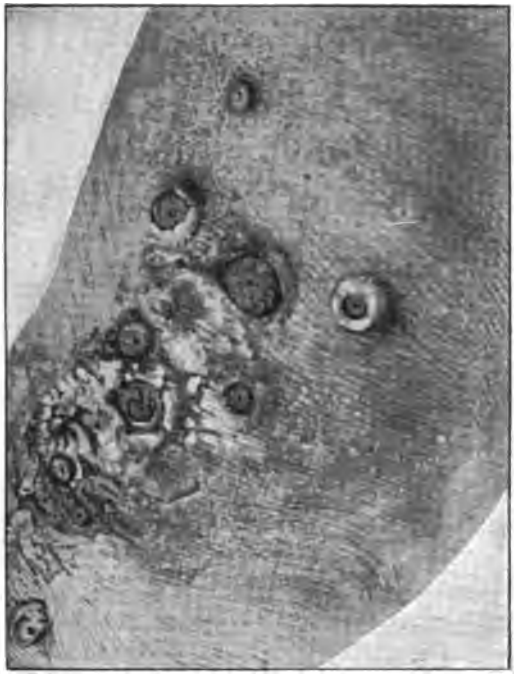

Fig. 162.—Chiggers in sole of foot.
(*From a photograph by Daniels.*)

During her gestation the chigger causes a considerable amount of irritation. In consequence of this pus forms around her distended abdomen, which now raises the inflamed integument into a pea-like

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elevation. After the eggs are laid (according to some, before this process) the superjacent skin ulcerates and the chigger is expelled, leaving a small sore which, if infected by any pathogenic micro-organism, as the bacterium of phagedæna or of tetanus, may lead to grave consequences.

Fig. 163.—Chigger lesions of hands and feet. (*From a photograph by Daniels.*)

Naturally, being nearest the ground, the feet are the parts most commonly infested by chiggers. The soles of the feet (Fig. 162), the skin between the toes, and that at the roots of the nails are favourite situations. Other parts of the body are by no means exempt; the scrotum, penis, the skin around the anus, the thighs, and even the hands (Fig. 163) and face, are often attacked. Usually only one or two chiggers are found at a time; occasionally they are present in hundreds, the little pits left after their extraction being some-

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times so closely set that parts of the surface may look like a honeycomb.

Treatment.—In chigger regions, houses, particularly the ground floors, must be frequently swept and accumulation of dust and *débris* be prevented. The housing of cattle and poultry must be similarly attended to. The floors should be sprinkled often with carbolic water, pyrethrum powder, or similar insecticide. Walking barefooted must be avoided. Bathing must be practised daily, and any chiggers that may

Fig. 164.—Chrysomyia macellaria, female.

have fastened themselves on the skin at once removed. They may be killed by pricking them with a needle, or by the application of chloroform, turpentine, mercurial ointment, or similar means, after which they are expelled by ulceration. The best treatment, however, is not to wait for ulceration, but to enlarge the orifice of entrance with a sharp, clean needle and neatly to enucleate the insect entire. Some native women, from long practice, are experts at this little operation. The part must be carefully dressed and protected until healed.

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MYIASIS.

THE SCREWWORM (*Chrysomyia macellaria*).

This is the larva of a dipterous insect (Fig. 164) common in certain parts (especially the tropics) of America, from

Fig. 165.—Chrysomyia macellaria, larva.

Fig. 166.—Native with Chrysomyia macellaria in nostrils and frontal sinuses; early stage. (*From a photograph by Daniels.*)

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Canada to Patagonia. The insect (9–10 mm. long) lays a mass of three or four hundred eggs on the surface of wounds, and in the ears and nasal fossæ of persons sleeping in the open air, especially of those having offensive discharges, which attract the fly. From these eggs the larvæ are hatched in a few hours. The latter are white, about three-quarters of an inch in length, and formed of twelve segments carrying circles of minute spirally arranged spines which give the creature a screw-like appearance; hence the vulgar name. They burrow in the tissues, devouring the mucous membrane, muscles, cartilages, periosteum, and even the bones, thereby causing terrible sores, and not unfrequently, particularly when they attack the ear or nasal fossæ, by penetrating to the brain, death. In thirteen cases collected by Laboulbène nine proved fatal; in thirty-one collected by Maillard twenty-one died.

If treated properly and in time by injections of chloroform, carbolic acid, turpentine, infusion of pyrethrum, and similar substances, the patient may be saved; neglected, he will most probably die. If necessary the frontal sinuses, the antrum, and other bony cavities must be opened to secure the expulsion of the larvæ.

In countries where this pest occurs bloody and offensive discharges from the nostrils should be carefully investigated, and, if found to be caused by the screwworm, vigorously treated.

VER MACAQUE (*Dermatobia cyaniventris*).

This is the larva of an American fly (Fig. 167) the identity of which, until it was studied by Blanchard, was doubtful.

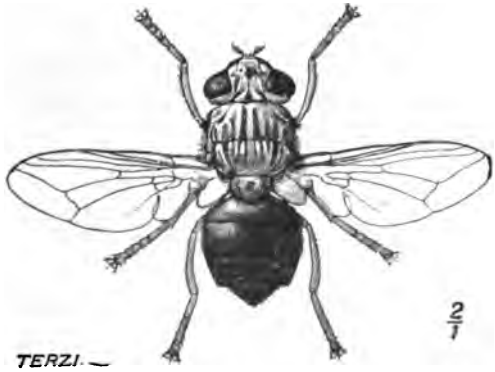

Fig. 167.—Dermatobia cyaniventris, female.

At an early stage the larva has the appearance represented by Fig. 168; at a later stage that represented by Fig. 169. The former stage of the larva is called *Ver macaque*; the

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latter, much larger, *Torcel* or *Berne*. At one time these two larval stages of the same insect were erroneously supposed to belong to different species.

Dermatobia cyaniventris measures from 14 to 16 mm. in length; it has a yellow head with very prominent brown eyes; the thorax is of a greyish colour, the abdomen of a dark

Fig. 168.—Dermatobia cyaniventris, larva, early stage. (*Blanchard.*)

metallic blue. It is widely distributed throughout tropical America, being especially common near wooded lands. It attacks the most diverse animals. Commonly it is found in cattle, pigs and dogs, but it occurs in the agouti, in the jaguar, in various monkeys, and in birds. It is rare in the mule, and writers have commented upon its absence from the horse. In man it has been reported from various regions of the body, namely, head, arm, back, abdomen, scrotum, buttocks, thigh, axilla. Its presence is accompanied by excruciating pains, especially at those times when the larva is moving.

It is supposed that when hatched out the larvæ penetrate the skin and produce an inflamed swelling about the aperture of entrance, from which a seropurulent fluid, containing the

Fig. 169.—Dermatobia cyaniventris, larva, later stage. (*After Brauer.*)

black fæces of the larva, exudes. Possibly it may reach the subcutaneous tissue by migration from the alimentary canal, as is the case in the allied European species, *Hypoderma bovis* (warble fly). Depied says that he has twice encountered this larva (the identity of which he ascertained by developing the insect) in the scalp of Tonquinese.

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VER DU CAYOR (*Ochromyia anthropophaga*).

Ochromyia anthropophaga measures from 8·5 to 11·5 mm. in length. It is of a yellowish-grey colour, with black spots on the abdomen. It was first reported from the district of Cayor, Senegambia, but it is probably widely distributed in tropical Africa. The larva burrows into the skin of man and beast, and produces a small inflamed swelling, from which it emerges in from six to seven days.

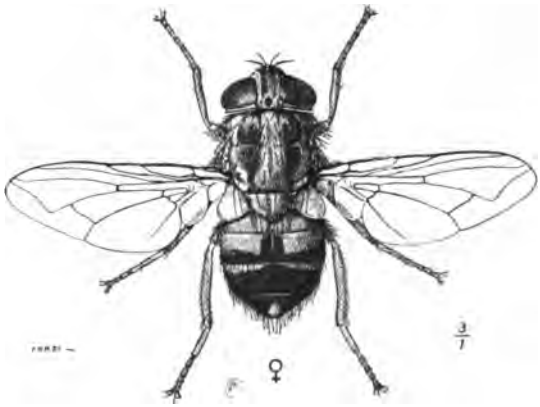

Fig. 170.—Cordylobia anthropophaga.

In Africa, and in many other parts of the tropical world, similar anthropophagous larvæ, which, however, have not yet been satisfactorily identified, are frequently encountered. According to Grünberg all these larvæ belong to one species—*Cordylobyia anthropophaga;* on the other hand, Gedoelst dis-

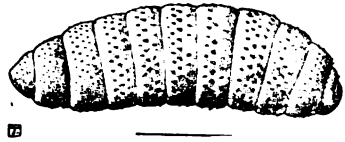

Fig. 171.—Ochromyia anthropophaga, larva.

tinguishes four distinct species — *Ochromyia anthropophaga*, *Bengalia depressa* (widely distributed), *Cordylobia anthropophaga* (German East Africa), and a larva of undetermined species—Lund's larva (Congo Free State).

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AUCHMEROMYIA LUTEOLA (Fabricius, 1805).

Synonym.—*Musca luteola.*

History.—*Auchmeromyia luteola* was first described by Fabricius in 1805 under the name of *Musca luteola.* In January, 1904, Captain Lelean described and figured this fly, which he had collected and reared from the larva while on service with the Anglo-French Boundary Commission in Northern Nigeria. He stated that the larva occurs as a cutaneous parasite on natives near Sokoto. In July of the same year, at the Oxford meeting of the British Medical Association, Dutton, Todd and Christy gave a more detailed account of the life-habits of this dipterous insect, and pointed out that in its larval stage it is a keen blood-sucker, and is known throughout the Congo as the "Congo floor maggot."

Fig. 172.—Auchmeromyia luteola, female.

Geographical distribution. — *Auchmeromyia luteola* is widely distributed throughout tropical Africa. On the west coast it ranges from Northern Nigeria to Natal. Dutton, Todd and Christy found it all over the Lutete and surrounding districts, and at Leopoldville. They were told that it is common at San Salvador, in Portuguese territory, and on the Congo at Matadi, in the cataract region, and at Tchumbiri, 150 miles above Stanley Pool. An intelligent native from Lake Tchad informed them that it was common in Western Tchad regions. It was found by Neave in the Soudan.

Specific diagnosis.—The fly measures from 10 to 12 mm. in length, and its body is rather stoutly built. The general colour is orange-buff, but numerous small black hairs give it a smoky appearance. The head is large, with eyes well separated in both sexes. The thorax shows two indistinct, dark, longitudinal stripes, which do not reach its posterior border. The abdomen differs in the two sexes, the second

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segment in the female being twice the length of the same segment in the male. The first segment has a narrow dark stripe on its hind margin in both sexes; the second segment in the male is marked by a broader band, tapering forwards along the middle line to the base of the segment. In the female the dark band is so wide that it occupies almost the whole segment. The third segment is almost entirely black in both sexes. The fourth is dark at the base and lighter posteriorly. The legs are the same colour as the rest of the body. The first tarsal joint is jet black, and stands out prominently against the large cream-white pulvillus. The wings are of a smoky-brown colour with conspicuous venation.

The larva is of a dirty white colour and semi-translucent. It consists of eleven very distinct segments, and when fully grown it measures about 15 mm. in length. The central part of the ventral surface is flattened. At the posterior margin of each segment are three short limbs transversely arranged and provided with spines directed backwards. These enable

Fig. 173.—Auchmeromyia luteola, larva.

the maggot to move about caterpillar-like and fairly rapidly. Laterally the segments bear two or more irregular protuberances, each of which has a posteriorly directed spine and a small pit. The anterior segment is roughly conical, and bears the mouth, which is placed between two black hooks protruding from its apex and curved backwards towards the ventral surface of the body. Paired groups of minute teeth are placed around the two hooks so as to form a sort of cupping apparatus. The last segment is larger, depressed, and turned upwards at an angle of about 45 degrees with the rest of the body; two spiracles open on its dorsal surface, which is surrounded by spines. The anus is placed in the anterior portion of its ventral surface, and behind it are two prominent spines. The alimentary canal commences with a short œsophagus, which ends in a proventriculus. A remarkable dorsal diverticulum, corresponding to the food reservoir of the muscid larva, opens into the œsophagus near its anterior end. After the larva has fed, the diverticulum is a very conspicuous object, being seen through the semi-transparent body wall as a bright red area, when full of blood extending from the head to about the fifth segment. The mid-gut is short; the

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hind gut is long, greatly coiled, and occupies the greater part of the body cavity. The maggot has a thick integument, which enables it to withstand a good deal of pressure without injury.

The duration of the larval period has not been determined. When ready to pupate, the larva selects a suitable spot and lies dormant. The puparium is a dark reddish-brown oblong body, measuring 9–10·5 mm. in length by 4–5 mm. in breadth. The anterior end is roughly conical; the posterior is rounded. The pupa stage lasts from two to three weeks.

The fly is usually found sitting motionless amongst the thatch, beams and cobwebs of the walls and roofs of native huts, but it is very difficult to see on account of its protective colouring, which corresponds exactly with the smoke-stained straw and rafters. It never bites, is usually silent, and deposits its eggs in the dust-filled cracks and crevices of the mud-floors of the huts, particularly in spots where urine has been voided.

The larvæ are found especially under the mats on which the natives sleep, in the floor crevices, and in moist soft earth at a depth of three inches or more. According to Bentley, as many as fifty could sometimes be found beneath a single mattress. They feed mainly or entirely at night, and they drop off at once if the limb on which they are feeding is moved. Those who sleep on beds or raised platforms are not attacked as a rule unless the bed be low, when the maggot may reach the occupant by crawling up either the supports or the grass wall against which the bed is usually placed. The natives state that the maggot is able to jump to a height of 18 inches, but this is unlikely.

LEECHES.

In the grass and jungle lands of many tropical and subtropical countries land-leeches, probably of special species, often occur in great abundance; so much so that in some circumstances they may prove to be something more than a nuisance. The *Hæmadipsa ceylonica* is one of the most active, as well as best known, of these. Before feeding, when outstretched, it is about an inch in length and about the thickness of a knitting-needle. It clings to a leaf or twig awaiting the passing of some animal, on to which it springs with remarkable activity. It at once attaches itself to the skin, and proceeds to make a meal on the blood. Animals are sometimes killed in this way; men even have been known to succumb to the repeated small bleedings by these pests. It is necessary, therefore, when passing through jungle

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lands in which leeches abound, to have the feet and legs carefully protected. The bite is not unfrequently the starting-point for a troublesome sore.

In the south of Europe and in the north of Africa the horse-leech, *Hæmopis sanguisuga*, sometimes gets into the gullet and nostrils of men as well as of animals. It has occasionally caused death by entering and occluding the air-passages. In Formosa I heard of and saw several instances of a similar form of parasitism, both in men and monkeys. To what particular species the leech in these cases belonged I do not know. Doubtless, when very young they were taken in unperceived with foul drinking water, and, wandering round the soft palate, found their way into the nose. Occasionally, in the cases I refer to, the animal would protrude from the nares and wander over the upper lip. For a long time they contrived to elude all attempts at capture. By dipping the face in cold water they could generally be persuaded to show themselves. In one instance the leech dropped out spontaneously. In another—an American naturalist who had been travelling much in the interior of Formosa, and who had suffered from severe headache and profound anæmia, the result of repeated epistaxis—I succeeded in removing the leech by attaching through a speculum a spring forceps to its hinder end, and afterwards injecting salt and water. It would be well, therefore, to bear in mind that in tropical countries persistent headache, associated with recurring epistaxis, may be caused by a leech in the nostril.

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SECTION VII.—LOCAL DISEASES OF UNCERTAIN NATURE

CHAPTER XLVII

CRAW-CRAW — CHAPPA — CLIMATIC BUBO— GOUNDOU—AINHUM—BIG HEEL—ONYALAI

CRAW-CRAW AND ULCERATING DERMATITIS

Most itching papular and pustular eruptions are termed kra-kra by the natives of the West Coast of Africa. Dr. John O'Neil describes under this name a pustular affection which he says is common in certain parts of the West Coast, and which he found to be associated with the presence of a filariform parasite in the papules. O'Neil says that this form of craw-craw resembles scabies; but he adds that symptoms subside in a cooler climate, to return, however, when the negro revisits the hot and damp atmosphere of his native country. The papules occur all over the limbs and body, either singly or in rings. In two days from its appearance the papule, he says, becomes a vesicle, and in two more a pustule.

On paring off the top of the papule with a sharp knife, and teasing up the little piece of integument in water, he found a number of minute filaria-like organisms wriggling about with great activity. Their activity speedily slowed down, and in a short time the worms died. These organisms, according to O'Neil's drawings and description, resemble somewhat *mf. bancrofti*. The measurements, however, do not quite correspond, the craw-craw filaria being shorter and broader ($\frac{1}{100}$ inch by $\frac{1}{2000}$ inch) than *mf. bancrofti*; moreover, unlike the latter, it presented two black markings at the cephalic end. He says that if the section of the papule be made sufficiently deep, five or six of these parasites may be seen in a field.

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Craw-craw is said to be contagious. It appears after an incubation period of three days, and is not curable by sulphur inunction.

O'Neil's observations have not been confirmed. I think it is quite possible that the parasite he found was one of the several blood filariæ we now know to be so common on the West Coast of Africa. It is comprehensible that in a country in which *mf. perstans* occurs in every second individual, it would be frequently found in such preparations as O'Neil examined. The removal of the top of a scabies papule would certainly be attended with some degree of hæmorrhage; in which case, should the patient chance to be the subject of any form of filarial infection, microfilariæ would be found in the preparation. Immersion in water would, as in the case of O'Neil's parasite, quickly kill the parasites. I do not wish to assert that O'Neil's parasite was *mf. perstans*, but the possibility of this must not be overlooked.

A disease resembling O'Neil's craw-craw was described some time ago by Prof. Nielly under the title "dermatose parasitaire." A French lad, who had never been abroad, became affected with a papulo-vesicular itching eruption resembling scabies, in which Nielly found a filariform parasite somewhat like that discovered by O'Neil in craw-craw. It had the same peculiar cephalic markings; in addition, it had a well-defined alimentary canal and rudimentary organs of generation. Nielly found nematode embryos in the blood in this case; so that we are justified in believing that the parasite in the skin was an advanced developmental form of the embryo in the blood, and that both were the progeny of a mature parental worm living somewhere in the tissues. Possibly Nielly's *dermatose parasitaire* and O'Neil's craw-craw were of the same nature.

Symptoms.—The term craw-craw is very loosely applied. Emily has described under this name a papulo-pustular skin affection which is common in certain parts of tropical Africa, and which is often the cause of much suffering to the traveller. It, or a similar disease, is by no means confined to Africa, for

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I have seen it in patients from India, and was at one time very familiar with it in South China. At the earliest stage the disease begins as an itching papule, very possibly at the seat of a mosquito bite. The itching provokes scratching, whereby some form of pyogenic micro-organism is inoculated. Pustulation follows, and is spread over feet and legs by soiled shoes and stockings and auto-inoculation. In this way an ulcerating, pustulating dermatitis is kept up. The veldt sore of South Africa, if not the same, is a similar disease.

Treatment.—Emily describes a very efficient treatment. Pustules are opened, crusts removed, and ulcers scraped. Boric acid powder is then dusted freely on the parts after a thorough scrubbing with sublimate lotion (1–1000), boricated vaseline applied on lint, and over all absorbent cotton and a bandage. The dressings are not disturbed for a week, when the parts will be found soundly healed. Such and similar auto-infective diseases of the hands and feet, so common in the tropics, I used to treat with a foot-bath of warm carbolic acid lotion (1–20), followed by dry dressing with abundance of boric acid powder, at the same time insisting on destruction of infected slippers, shoes, and stockings.

CHAPPA.

Under the name "chappa" Read describes a disease which he has met with in the western district of the colony of Lagos. During two and a half years he has seen six examples, two in males, four in females. He thus describes it:—

"The patients all give the same history. The disease commences with severe pains in the limbs, muscles, and joints. After a few months the pain decreases, and some joints begin to swell and convey the sense of fluctuation. About the same time nodules develop in different parts of the body. These nodules are in the subcutaneous tissue, and are about the size of a pigeon's egg. After a time, without the formation of an abscess, the skin over the nodule ulcerates and exposes a circular or oval ulcer with a

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fatty-looking base. The nodules may be single, but are more often multiple, and may be so close together that when ulceration ensues the ulcers coalesce, forming a serpiginous ulcer. Sometimes the nodules are absorbed without proceeding to ulceration. The ulcers are very chronic and last for years, sometimes healing at one place and gradually extending in another. The joints I have seen most affected are the knee, elbow, and wrist. The sense of fluctuation was so marked in one case that I opened the joint; but no fluid exuded, a fatty-looking material protruding through the incision. The disease after a time attacks the bones, and the joints may become totally disorganised." (*Jour. of Trop. Med.*, October 15th, 1901.)

On comparing the photographs illustrating Read's paper with others of a very similar complaint common among the natives in certain parts of British East Africa, I am inclined to think both sets of photographs represent identical conditions. Possibly "chappa" is a tertiary phase of yaws.

Treatment.—Neither potassium iodide nor mercury avails. Scraping, escharotics, and antiseptics seem to be more effective; but, although the disease may heal under treatment in one place, it breaks out in another.

CLIMATIC BUBO.

Scheube has applied the term "climatic bubo" to a type of non-venereal adenitis not uncommon in tropical climates. So far as available statistics show, the disease is specially prevalent among the crews of warships on the eastern coast of Africa. It occurs also in the Straits of Malacca, in China, where I have seen a fair number of cases both in landsmen and in sailors, in the West Indies, Japan, the Mediterranean, and probably in many other places, including, perhaps, in a minor degree, Europe. It appears to be epidemic at times in certain places, and to prevail in groups of individuals living under similar hygienic conditions. Thus, Ruge reports thirty-eight cases in the German squadron blockading the Zanzibar coast in 1888–89; Godding notes its frequency in the

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British fleet, also on the East African coast; Skinner mentions forty-nine cases occurring in a regiment and battery of artillery: of these, twenty-eight developed in Calcutta, thirteen in Hong Kong, four in England, two in Allahabad, and two in Malta.

Symptoms.—The disease generally commences with fever of a remittent type in association with inflammatory swelling, usually of a sub-acute character, of the groin glands. The oblique inguinal glands are those most frequently affected, but at times it is the crural glands that are attacked. Sometimes both groins are affected, sometimes only one, sometimes one groin is attacked after the other. The affected glands slowly or more rapidly enlarge to the size of a hen's egg, or even larger. After several weeks, it may be months, the swelling gradually subsides. Occasionally the periglandular connective tissues inflame, the integuments become adherent, and suppuration ensues. If the suppurating glands be freely incised, or excised, the parts readily heal; but if they are left alone, or inefficiently treated, fistulous tracks form and may take a very long time to heal.

Hitherto no satisfactory explanation of this type of adenitis has been forthcoming. No special bacterium has been demonstrated in the tissues. There are no adequate reasons for supposing, as has been conjectured, that the disease has any connection with plague, or that it is a form of pestis minor. Most probably the adenitis depends on some virus which had been introduced through an overlooked wound or insect bite on the legs or genitals.

Treatment should consist in rest and soothing applications during the more acute stage. After pain and tenderness have subsided, graduated elastic pressure should be applied. Concurrent malaria would call for quinine; syphilis, for mercury or the iodides.

GOUNDOU OR ANAKHRE (*Gros Nez*).

On December 10th, 1882, Professor A. MacAlister read a paper before the Royal Irish Academy on what were termed the horned men of Africa. In the

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British Medical Journal of December 10th, 1887, Lamprey gave further details, illustrated with drawings, on the same subject. He had seen three such cases on the West Coast of Africa, all of them Fantees; one came from the Wassau territory, one from the Gamin territory, the third was a visitor to Cape Coast Castle. Renner also reports and illustrates a case from the Sierra Leone river.

Maclaud calls attention to what is manifestly the same affection, which, according to him, occurs

Fig. 174.—Goundou.

Fig. 175.—Goundou.
(*From Photograph in the Journ. of Trop. Med.*).

in a considerable proportion—one or two per hundred—of the inhabitants of certain villages on the Ivory Coast. The natives call it *goundou*, and, also, *anakhre*. Maclaud says it is confined to the riverain districts of the lower Camoe; according to the information he received, if found elsewhere it is only in individuals who had previously resided in this district. Lamprey's and Renner's observations prove that goundou has a considerably wider distribution.

Symptoms.—According to Maclaud, the disease usually commences soon after childhood, although adults also may be attacked. The earliest symptoms are severe and more or less persistent headache which, after a time, is associated with a sanguino-purulent discharge from the nostrils, and the forma-

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tion of symmetrical swellings the size of a small bean at the side of the nose. Apparently the swelling affects the nasal process of the superior maxilla The cartilages are not involved. Although Maclaud does not refer to this point, it may be assumed that the nasal ducts remain patent. After continuing for six or eight months, the headache and discharge subside. Not so the swellings; these persist and continue slowly and steadily to increase until in time they may attain the size of an orange, or even of an ostrich's egg. As they grow,

Fig. 176.—Goundou in a West Indian child. (*Dr. Henry Strachan.*)

the tumours, encroaching on the eyes, may interfere with the line of vision and finally destroy these organs. There is no pain in the tumours themselves. The superjacent skin is not involved, being healthy-looking and freely movable. The tumours are oval, with the long axes directed downwards and slightly from within outwards. Lamprey's drawings give a more elongated form and horizontal direction. The swellings, according to Maclaud, when of moderate dimensions, look something like two half-eggs laid alongside the nose, one on each side. The

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nostrils are bulged inwards, and more or less obstructed; but, in the later stages at all events, there is no discharge, neither can any breach of the mucous surface be detected. The hard palate is not affected in any way.

Maclaud had no opportunity of ascertaining by *post-mortem* examination, or by surgical operation, the nature of this singular disease. He inclines to the opinion that, in the first instance, the process is started by the larvæ of some insect which find their way into the nostrils. I would point out, however, that the symmetry of the growths is difficult to account for on this hypothesis. Maclaud observed a similar affection in a chimpanzee.

Strachan records and illustrates (Fig. 176) an instance of goundou in a West Indian negro child. In this case the swellings were congenital, and had only increased in proportion to the child's growth. They were hard, smooth, bony masses, somewhat of the shape and size of an elongated pigeon's egg, and sprang from the nasal process of the superior maxillary and nasal bones. For æsthetic reasons they were removed by the chisel, and were found to consist of compact bone with a cancellous core. Strachan states that he had seen two similar cases, and had often noted a "ridge" in this part of the face of West Indian negroes. He suggests that the condition may be an example of atavism, referable to some tribal peculiarity of the original West African stock.

Chalmers has given an admirable and well-illustrated account of this affection as seen on the Gold Coast, where it is fairly common and is known as "henpurge." He confirms Strachan as to the anatomical characters of the swellings, which he regards as the result of an osteoplastic periostitis due to yaws. He affirms that the morbid process begins during, or soon after, an attack of yaws, and is correlated in some way to an anatomical arrangement of the blood-vessels of the parts, an arrangement which, he gives the reader to infer, is peculiar to the negro of this part of Africa.

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AINHUM.

This is a disease of a very peculiar character, affecting the toes, particularly the little toes, of negroes, East Indians, and other dark-skinned races.

Symptoms.—The disease commences as a narrow groove in the skin almost invariably on the inner and plantar side of the root of the little toe. It may occur in one foot only, or in both feet simultaneously, or it may affect one foot after the other. The groove, once started, deepens and extends gradually round the whole circumference of the toe. As the groove deepens—it may be, though not necessarily, with some amount of ulceration — the distal portion of the member is apt to swell to a considerable size, as if constricted by a ligature. There is little or no pain, although there may be inconvenience from the liability to injury to which the dangling and now everted toe is exposed. In the course of years the groove slowly deepens, and finally the toe drops off or is amputated. The groove may either correspond with a joint or it may be formed over the continuity of a phalanx. In rare instances, after the two distal phalanges have dropped off or been amputated, the disease recurs in the stump, and the proximal phalanx in its turn is thrown off. Of the other toes the fourth is the one which is most frequently affected; very rarely are the third, or second, or great toes attacked. In the Army Medical Museum at Washington, U.S.A., there is a wax model representing a case of this or a similar affection, in which all the toes had been thrown off and the disease was making progress in the leg.

Fig. 177.—Ainhum.

Ainhum is very rare in women or children, being

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most common in adult males. It runs its course in from one to ten or even more years.

On section it is found, as a rule, though not invariably, that the panniculus adiposus of the affected toe is much hypertrophied, that the bone is infiltrated with fatty matter, and that the other tissues are correspondingly degenerated. Sometimes the bone is thinned, or even altogether absorbed. At the seat of constriction a line of hypertrophy of the epithelial layers, and of atrophy of the papillary layer of the skin, together with a band of fibrous tissue more or less intimately connected with the derma, surround, in whole or in part, the narrow pedicle.

Nothing is known as to the true nature and cause of this disease, to which the European and white-skinned races are not, but to which the African races, particularly the negroes of the West Coast, are specially liable. Some have suggested that it is a trophic lesion depending upon some nervous affection. The occurrence of severe loin pains, which Dupouy says he remarked at the commencement in some of his cases, as well as the tendency of the affection to run in families, as noted by Da Silva Lima, afford a certain amount of support to this view. Others suggest that it is a manifestation of leprosy; others that it is a form of sclerodermia; others, again, and on equally inadequate grounds, that it is produced artificially by intentional ligation or by the wearing of toe rings. My own impression is that it is provoked, at all events in the first instance, by wounds—so easily inflicted on bare feet in walking through grass or jungle. The fold of skin in which the lesion of ainhum commences is very liable, especially in the splayed-out toes of the negro, to be wounded in this way. If we examine the under surface of the joint flexures of the toes in many individuals of this race, even of those not affected with ainhum, we often find the skin, particularly at the proximal joint of the little toe, thick, rough, scaling, and sometimes even ulcerated. One can understand that continual irritation of this sort, produced and kept up by wounds from sharp grasses or jiggers (Wellman), would in time give

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rise, especially in the dark-skinned races so prone to cheloid, to fibrotic changes in the derma, which might very well end in a sort of linear cicatricial contraction and ultimately in slow atrophying strangulation of the affected member. The disease is said, however, to have been seen in those who wear shoes; but, unless it could be shown that such individuals had always worn shoes, this objection to the explanation offered would not apply. I have seen a negro in whom the entire integument of the little toe was involved in a sclerodermia, and the part in consequence was shrunken and hidebound, whilst the little toe of the other foot was affected with well-marked ordinary ainhum; the process was diffuse, as it were, on the one side, localised on the other.

The tail in certain species of monkey is liable to a similar disease. I have had under observation for some time a pet monkey in which the part corresponding to the distal vertebra dropped off in consequence of an ainhum-like linear constriction. Two months later the next vertebra was similarly amputated, and later a third groove formed a little higher up the tail.

Treatment.—It has been suggested that division of the constricting fibrous band would delay the evolution of the disease. In the early stage this might be tried. When troublesome, the affected toe should be amputated.

BIG HEEL, OR ENDEMIC HYPERTROPHY OF OS CALCIS.

MacLean (*Journ. of Trop. Med.*, Nov. 1, 1904) describes a peculiar form of enlargement of the os calcis which he observed at Kaziankor, Gold Coast, West Africa, among Fantis and Kroos. The disease begins somewhat suddenly, being preceded by fever and accompanied by pain and tenderness which reach their maximum in about a month, gradually diminishing during the succeeding one or two months. Concurrently with the pain a swelling of the external surface of the os calcis, rarely of the tarsal bones, makes its appearance. Sometimes one heel only, sometimes both heels are affected. The swelling may

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be so considerable as to be quite evident both to touch and sight. It subsides to a certain extent, though not altogether, as the pain diminishes. Locomotion is seriously interfered with by the pain, but there is no implication of joints. The disease relapses from time to time, more especially during the rainy season. In one case recorded by MacLean severe pain could be provoked at any time by application of cold water.

Maxwell (*Journ. of Trop. Med.*, March 15, 1905) reports a similar condition in natives of Formosa. As in MacLean's cases, the patients were young adults from 20 to 25 years of age. In Maxwell's cases the disease, although very painful, seemed to be of a more chronic character. In one instance the patient's sufferings were much relieved by trephining the affected bones. This curious condition somewhat resembles goundou. So far, we have no clue to its ætiology. It is probably not syphilitic. Iodide of potassium did not relieve Maxwell's cases.

ONYALAI.

Yale Massey describes (*Journ. of Trop. Med.*, Sept. 1, 1904, April 1, 1907), under the above title, a peculiar disease occurring among the natives of Portuguese West Africa, and also on the Lualaba River. It is characterised by the formation of a number of vesicles, distended with blood, from $\frac{1}{4}$ to $\frac{1}{2}$ inch in diameter, on the hard palate and on the inside of the cheeks. Some of the vesicles are umbilicated. They differ from ordinary blood blisters by the presence of numerous trabeculæ and the semi-coagulation of the contents; this makes the vesicle difficult to empty. The urine apparently invariably contains free blood. Occasionally the disease is accompanied by fever, and although with one exception all Yale Massey's cases recovered within a week to ten days, the natives regard the disease with dread owing to its reputation for deadliness. The ætiology is quite unknown.

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Appendix

THE PROTOZOA OF THE BLOOD OF VERTEBRATES

RECENT discovery has clearly demonstrated the importance of the Protozoa as factors in the ætiology of disease, especially of tropical disease.

Manifestly the subject is still in its infancy. Many as yet unknown species of blood protozoa will doubtless be added to the already considerable list of those attacking man and the lower animals. As regards man, it is doubtful if we have as yet completed the list even of the much-studied malaria parasites, much less determined their respective life histories and zoological relationships. Moreover, there are certain genera of blood protozoa which, although occurring in other mammals, have, so far, not been found in man, Babesia and Hæmogregarina for example. It is not unreasonable to conjecture that, although hitherto unrecognised, representatives of these genera do occur in man, and that ere long they will be discovered. The investigator must not lose sight of this probability.

The entire subject is one of the utmost importance to the medical man in the tropics, and, whether he would perfect himself in existing knowledge or seek to add to it, he should study it practically and from the standpoint of comparative pathology. I would therefore strongly recommend him to avail himself of the abundant opportunities he is sure to enjoy to study the blood protozoa not in man only but in other mammals, in birds, in fishes and in reptiles. As a guide and help in such studies I append a list—complete up to date—of known species of blood protozoa, together with, in condensed form, an account of all that is really known of their structure and life history.

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As the number of known species is already so considerable, some sort of classification of the blood protozoa is desirable. Unfortunately our knowledge is not sufficiently full to allow of any classification that might be considered final. In former editions of this book I followed Laveran, who divides the *Hæmocytozoa* (= *Hæmosporidia*) into three genera, namely (1) *Hæmamœba* (= *Plasmodium*), (2) *Piroplasma* (= *Babesia*), (3) *Hæmogregarina*. This classification has become inadequate. Moreover, not only the classification of the Hæmosporidia, but that of the entire phylum Protozoa may have to be completely recast. Recent observations show that many forms, such as *Herpetomonas*, *Trypanosoma*, *Trypanoplasma*, hitherto grouped in a separate class, *Mastigophora*, or *Flagellata*, and indeed even the *Spirochæta* which many still group amongst the *Bacteria*, represent, at all events in some instances, merely developmental stages of other forms called *Hæmamœba*, *Hæmoproteus*, *Hæmogregarina*, *Babesia*, *Leishmania*, etc., and grouped in the class Sporozoa. As a tentative arrangement, I here propose a classification suggested by Sambon.

CLASSIFICATION OF THE BLOOD-INHABITING PROTOZOA

HÆMOPROTOZOA, SAMBON, 1907.

Synonyms.—*Hæmocytozoa* Danilewsky, 1885, *pro parte*; *Hæmosporidia* Mingazzini, 1890, *pro parte*; *Hæmamœbidæ* Ross, 1899, *pro parte*; *Trypanosomidæ* Doflein, 1901, *pro parte*.

Parasitic protozoa of complicated life history, inhabiting the blood plasma or the blood cells of vertebrates (intermediary hosts) during a "vegetative cycle" characterised by non-sexual multiplication (*schizogony*), and the body of blood-sucking invertebrates (definitive hosts) during a "sexual cycle" characterised by sexual reproduction (*sporogony*).

In the blood of the vertebrate, the young parasite (*schizont*) * multiplies asexually by fission or gemmation into two or more segments (*merozoites*). † This process of multiplication may be repeated for an indefinite number of times, but sooner

* *Amœbula, myxopod, trophozoit.*

† *Enhæmospores.*

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or later some of the merozoites develop into new forms (*sporonts*), which are destined to pass into the body of the definitive host and carry on the further life of the parasite. These sporonts become sexually differentiated (*gametocytes*), sometimes within the blood of the intermediary host, in other cases only after reaching the gut of the definitive host. When sexually differentiated they cease to break up into merozoites. As a rule they become encysted within the host cell and remain quiescent until removed from the blood. The female cells (*macro-* or *megagametes* = ♀) are characterised by a more compact cytoplasm which is full of food reserve material and stains more deeply than the cytoplasm of the asexual cells (☿). The male cells (*microgametocytes* = ♂) are characterised by a much larger nucleus, rich in chromatin, and by a hyaline cytoplasm without reserve material which stains more faintly than that of the asexual cells. In many cases, when the schizonts inhabit the erythrocytes, their cytoplasm becomes filled with minute granules of dark material (*hæmozoin* *), an excrementitious product. These granules are larger and more abundant in the sporonts. The gametocytes do not conjugate within the body of the vertebrate host. If not withdrawn within a certain time, the microgametocytes degenerate. The macrogametes, on account of the reserve nutriment stored up in their cytoplasm, may persist for a longer period, and, according to Schaudinn, under favourable conditions may even revert to the schizogonic type and reproduce asexually (*parthenogenesis*) the various forms (☿, ♀, and ♂). Having reached the alimentary tube of an appropriate definitive invertebrate host, the macrogametes are fertilised by the spermatozoa (*microgametes*) which are produced by the microgametocytes or sperm-mother-cells. The fertilised female cell (*zygote* or *copula*) becomes an elongated pyriform and actively motile body (*oökinete* †) which may remain free or become encysted (*oöcyst*). In either case, by repeated division, it gives rise to a number of minute elongated forms (*sporozoites* ‡), in certain instances (*Hæmogregarinidæ*) in secondary cysts or spore bags (*sporoblasts*) formed within the oöcyst. Ultimately the sporozoites migrate to the mouth parts of their invertebrate host to be inoculated into the blood of a suitable vertebrate. In certain instances, possibly in all, though this is not proved, some of the sporozoites lodge within the ova of the invertebrate host and await the development of the progeny of this host to pass into their appropriate intermediary. In some cases this appears to be the usual mode of transmission.

The Hæmoprotozoa may be provisionally divided into the

* The term "hæmozoin" is here suggested instead of "melanin," which has a definite physiological meaning. The term "black pigment" is vague and incorrect.

† *Vermicule.*

‡ *Exotospores, blasts, gametoblasts.*

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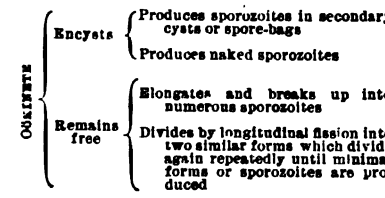
following four families or groups, distinguished principally by differences in the development of the oökinete *—



1. Hæmogregarinidæ. Neveu-Lemaire, 1901.

Synonyms. — *Hæmosporidia* Labbé, 1894; *Hæmosporea* Minchin, 1903.

Schizont endocellular (in erythrocytes, or in leucocytes, or indifferently in either, or in tissue cells); globular, oval or club-shaped; slightly amœboid; does not produce hæmozoin. The mature schizont may entirely occupy its host-cell, which is reduced to a mere shell (*cytocyst*) with the hypertrophied and flattened nucleus adherent. *Schizogony* within the host-cell, either by longitudinal fission into 2, 4 or 8 merozoites arranged meridionally like the staves of a barrel, as in *Adelea ovata* and other Coccidia, or by multiple segmentation. In the latter case, in the same species, the cytocyst may enclose a few large merozoites (*macromerozoites*) or numerous small merozoites (*micromerozoites*). Possibly this dimorphism, also witnessed in the schizogony of *Plasmodium danilewskyi*, and, to a less extent, in other Plasmodidæ, may, as in the Coccidia, indicate an early sexual differentiation, true gametocytes being preceded by one or more generations of sporonts multiplying by schizogony. Close to the nucleus of the division forms, a small chromatin mass (blepharoplast?) has been described in certain species (*H. quadrigemina*, *H. blanchardi*). Schizogony may occur in the peripheral circulation (*H. simondi*, *H. bigemina*), but more frequently it is limited to the internal organs (liver, spleen, lungs, kidney, brain, bone marrow), and may be confined to one selective organ as the liver or the bone marrow (*H. canis*).

Sporont endocellular, enclosed when full grown in a sausage-shaped, bean-shaped or gourd-shaped capsule which may be quite thick (*H. canis*) and opaque, or exceedingly thin and transparent. In some cases the parasite appears to be lying merely in a kind of cavity within the cytoplasm of its cell-host. In other cases the capsule is unmistakable, as in *H. mirabilis* and *H. tunisiensis*, where in specimens stained by the Romanowsky method it presents a stippling of red dots

* This grouping is merely tentative. Our knowledge of the development and life history of most forms is so very scanty and uncertain that it is at present impossible to frame any definite classification.

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which show it up very distinctly even after the escape of the parasite, whether within the erythrocyte or shrivelled up in the liquor sanguinis. At one or both extremities the capsule usually presents a transverse line suggestive of the existence of an operculum (Fig. 178). The quiescent parasite within is invariably club-shaped (*vermicule*), but may be either slender and more or less elongate, or thick and short. The wider, rounded extremity is the anterior end of the body and presents at its apex a tiny beak-like projection apparently retractile (Fig. 179). The attenuated posterior extremity is usually sharply flexed on the body. The recurved portion may be very short and resemble the hook of a knitting needle, or it may be equal in length to the anterior portion, giving the doubled parasite the appearance of a compressed letter U. In some species (*H. mesnili*) the encapsuled sporonts become greatly elongated and more or less coiled within their cysts. The nucleus is usually median, but it may approach one or other extremity; it varies greatly in size, shape, and in the arrangement of its chromatin. The cytoplasm may be hyalin or granular, the staining reactions varying accordingly. Chromatoid granules are frequently seen irregularly disposed, but chiefly in the posterior part of the body. Some-

Fig. 178.—H. seligmanni: encysted sporont, showing operculate capsule. (*After Sambon.*)

Fig. 179.—H. seligmanni: free sporont. (*After Sambon.*)

times the cytoplasm presents one or more vacuoles. Sexual differentiation is not always manifest, but in several species (*H. lacertarum*, *H. rarefaciens*, *H. platydactyli*) we find, besides the indifferent sporonts, two forms corresponding more or less in structure to the gametocytes of the Plasmodidæ.

Very frequently, especially if the blood has not been dried and fixed rapidly, a number of the sporonts may be found free in the plasma. Examined in the living state, these free parasites exhibit active gregarinoid movement. As a rule, they glide along in a steady continuous manner. Sometimes constrictions and swellings seem to pass like waves along the body; hence if killed and fixed in the act of contraction they may present a moniliform appearance.

In vitro, the sporonts after escaping from their host-cells and capsules may be seen to re-enter fresh erythrocytes, suggesting that something of the same sort takes place in the gut of the invertebrate host.

The action of the parasite on its host-cell varies greatly. Some species do not seem to produce any injurious effect. Usually, the growing parasite displaces the nucleus, and, when of large proportions, may distend and distort the cell. Other

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species expand, or attenuate, or even disrupt the host-cell and elongate, flatten or fragment its nucleus. The erythrocytes occupied by *H. viperina*, like those enclosing *Plasmodium vivax*, present numerous Schüffner's dots when deeply stained by the Romanowsky method.

Sporogony has been reported to occur in insects (Christophers), in ticks (Schaudinn, Durham, Christophers), and in leeches (Siegel, Billet, Brumpt), but nothing definite is known as to the actual process. According to Siegel and Christophers, two sporonts, apparently alike or more or less clearly differentiated into male and female, associate, become encysted and give rise to sporoblasts each containing a number of sporozoites. (See *H. gerbilli*, *H. canis*, *H. stepanovi*, *H. bagensis*, *H. lacertarum*, *H. minima*, *H. simondi*.)

Until quite recently, authors divided the Hæmogregarinidæ into three genera based chiefly on the relative proportions of the parasite and the host-cell.

I.—*Lankesterella* Labbé (= *Drepanidium* Lank.). Parasite not more than three-fourths the length of the host-cell. Parasitic in amphibia.

Fig. 180.—H. gerbilli; oöcyst containing sporoblasts. (*After Christophers.*)

II.—*Karyolysus* Labbé. Parasite not exceeding the host-cell in length and invariably exercising a destructive influence on the cell nucleus. Parasitic in lizards and snakes.

III.—*Hæmogregarina* Danilewsky s. str. (= *Danilewskya* Labbé). Parasite exceeding the host-cell in length and doubled up within it. Parasitic in tortoises, turtles, crocodiles, fishes, lizards and snakes.

This classification has proved quite inapplicable; therefore, until we know more about their life history and development, the numerous organisms which make up the group Hæmogregarinidæ had better be arranged, as suggested by Lühe, according to the different orders of hosts under the collective name *Hæmogregarina*.

Hæmogregarines of Mammals.

H. gerbilli Christophers, 1905. In erythrocytes of Indian field rat *Gerbillus indicus*. Sporont encysted, club-shaped

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posterior extremity acuminated and sharply flexed on body. Nucleus median. A few chromatoid granules chiefly at posterior end. Host-cell enlarged, misshapen, dehæmoglobinised. Schizogony not seen. In 1905 Christophers believed he had discovered the sexual cycle of *H. gerbilli* in the rat louse, *Hæmatopinus stephensi* Christophers and Newstead. He described large oöcysts, 10 to 350 μ diameter (Fig. 180), in the body cavity of the insect, which produced oval sporoblasts enclosing six to eight sausage-shaped sporozoites 15 μ long by 4 μ broad. In a later paper, however, he expresses a doubt as to whether these cysts have anything to do with the hæmogregarine.

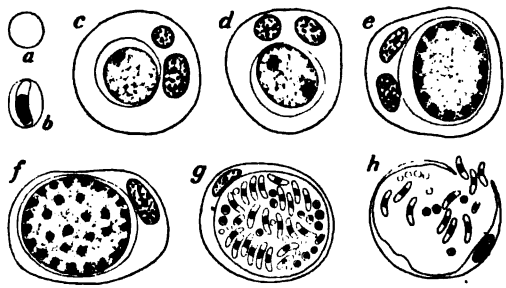

Fig. 181.—H. jaculi: *a*, normal erythrocyte of jerboa; *b*, sporont; *c-h*, schizogony within liver cells. (*After Balfour.*)

H. jaculi (Balfour, 1905) (= *H. balfouri* Lav.), Fig. 181. In the jerboa or desert rat, *Jaculus gordoni* at Khartoum; *J. orientalis* at Tunis. Schizogony within liver cells by multiple division. Cytocysts 21 to 23 μ in diameter enclosing 16 to 30 sausage-shaped merozoites. Sporont club-shaped, encysted in erythrocytes. Sporogony unknown.

H. bovis Martoglio and Carpano, 1906. In erythrocytes of oxen (*Bos taurus*) in Abyssinia. Sporont club-shaped 7 to 10 μ long by 1·6 to 2 μ broad. Schizogony and sporogony unknown.

Fig. 182.—H. canis: endocellular and free sporonts. (*After Wenyon.*)

H. canis (James, 1905) (= *Leucocytozoön canis*), Fig. 182. In pariah dog, *Canis familiaris*, in Assam, India, and Perak, Federated Malay States. Schizogony in bone marrow by multiple fission.

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Cytocysts spherical or oval measuring up to 48 μ in diameter and enclosing about 30 sausage-shaped merozoites. Schizont round (9 μ) or oval (12 μ by 8 μ) in mononuclear leucocytes in bone marrow, not encysted; rarely seen in peripheral circulation. Sporont in transitional or polymorphonuclear leucocytes, club-shaped, doubled within thick distinct capsule 10 to 12 μ long, 4·2 to 5·2 μ broad. Host-cell slightly enlarged, nucleus displaced and fragmented. Sporogony—Gerrard suggested that it might occur in ticks, and Christophers claims to have followed it in *Rhipicephalus sanguineus* (Latreille) from infected dogs. Within the tick's gut, the sporonts escape from their capsules and lodge themselves in the large cells of the gut; here they multiply by fission and give rise to sexually differentiated forms which conjugate and become encysted. The resulting oöcyst attains a diameter of 14 μ. Further development is uncertain. The method of re-entering the dog was not elucidated. The sexual cycle of *H. canis* seems to take place solely in the adult female ticks. In the larva and in the male tick Christophers was unable to trace any development. In the nymph the parasites exhibit the early stages of development, but completely disappear by the fourth day.

H. felis Christophers, 1906. Found by Patton in polymorphonuclear leucocytes of bazaar cat (*Felis catus domestici*, L.) about Madras. Sporont similar to that of *H. canis*, capsule much thinner. Schizogony and sporogony unknown.

H. funambuli (Patton, 1906) (= *Leucocytozoön funambuli*). In mononuclear leucocytes of the five-striped palm squirrel, *Funambulus pennantii* Wroughton at Kathiawar and Gujarat, India. Sporont club-shaped and doubled up in thin capsule 10 μ by 5 μ. Free sporont 13-14 μ by 3-4 μ. Host-cell stains faintly, nucleus often fragmented. Schizogony and sporogony unknown.

H. muris (Balfour, 1905) (= *Leucocytozoön muris*). In mononuclear leucocytes of sewer rat, *Mus decumanus*, at Khartoum. Sporont 9·10 μ by 4·5 μ. Schizogony and sporogony unknown.

HÆMOGREGARINES OF REPTILES.

A.—CROCODILIA.

H. kankini Simond, 1901. In erythrocytes of Gavial, *Gavialis gangeticus* (Gmel.) India. Schizogony in lungs. Cytocyst 20 μ diameter, enclosing 30-40 merozoites. Sporogony unknown.

H. crocodilinorum Börner, 1901. In broad-fronted crocodile, *Osteolæmus tetraspis* Cope (= *Crocodilus frontatus* Murr.). Börner ascribes to this same species a hæmogregarine found in the alligator, *Alligator mississippiensis* Daud.

Similar forms have been found in the long-nosed crocodile, *Crocodilus cataphractes* Cuv., and by Minchin, Gray and Tulloch in the crocodiles of the Victoria Nyanza.

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B.—CHELONIA.

H. stepanovi Danilewsky, 1889 (Fig. 183). In the European pond tortoise, *Emys orbicularis* L. Schizogony in bone marrow, liver, and, more rarely, in the spleen. Cytocyst oval, 10-16 μ by 4-6 μ, enclosing rarely more than 10 merozoites arranged irregularly or like the staves of a barrel. Free merozoites, 6-8 μ, elongate, club-shaped and slightly arched, but may assume various forms (fusiform, oval or even round). They have a comparatively large, oval nucleus. Sporont club-shaped; doubled up and encysted, 15-18 μ long; if free and outstretched, 30-40 μ long. Nucleus at bend, sometimes elongated. Cytoplasm may present unstaining, light refracting granules or vacuoles. Two parasites may be found within the same erythrocyte. Host-cell ultimately destroyed. Its nucleus

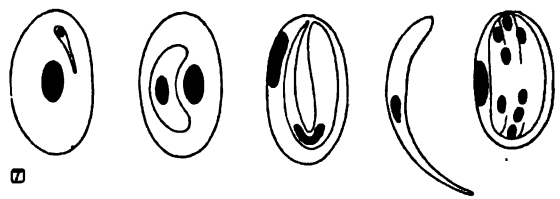

Fig. 183.—H. stepanovi. (*After Laveran.*)

may then remain attached to encysted parasite. Sporogony, according to Siegel, in a leech, *Placobdella catenigera* (Moqu. Tand.). So long as the imbibed blood remains stored in a concentrated form within the diverticula of the leech's stomach the encysted sporonts remain quiescent. To witness a change we must examine that minute quantity of blood which passes each day into the intestine. Here the erythrocytes are destroyed and the hæmogregarines liberated. The free sporonts penetrate between the cells of the intestinal wall and become differentiated into male and female forms. The microgametes are exceedingly small. After fertilisation, the oökinetes pass into the blood sinuses which embrace the intestine and finally reach the pharyngeal glands. Here they settle, become round (oöcysts) and enlarge considerably. Meanwhile their contents break up into numerous sporoblasts, each one of which contains a number of sporozoites. Finally the cysts burst and the sporozoites, in the shape of spirally wound threads, may be seen within the lumen of the gland awaiting to be transmitted to other tortoises during the act of sucking. Some of the oökinetes, instead of migrating to the pharyngeal glands, seem to pass to the ova. Siegel found sporozoites in the hardly developed glands of immature leeches which were still feeding on the yolk.

H. labbei Börner, 1901. In erythrocytes of *Chrysemys*

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scripta (Schoepff.), var. *elegans* (Wied.) (= *Clemmys elegans*, Strauch). Also in *Platemys* sp.

H. laverani Simond, 1901. In *Emyda granosa* (Schoepff.). Early amœboid forms 3-5 μ in diameter. Sporonts characterised by the presence of two refracting granules. Schizogony and sporogony unknown.

H. mesnili Simond, 1901. In *Kachuga tectum* (Gray) (= *Emys tectum*). Schizogony in internal organs. Sporont 30 μ long when fully outstretched. Within capsule it forms three branches of equal length variously interlaced. Sporogony unknown.

H. billeti Simond, 1901. In *Trionyx cartilagineus* (Boddert) (= *T. stellatus* Geoffr.). Schizogony in peripheral circulation by multiple fission (rosette formation). Schizonts in all stages of segmentation and finally divided into numerous more or less oval merozoites. Sporont club-shaped. Host-cell nucleus displaced.

H. stepanoviana Laveran and Mesnil, 1902. In *Damonia reevesii* (Gray). Schizogony in liver. Sporonts outstretched 18-20 μ long by 5 μ maximum breadth at anterior extremity. Nucleus oval with long axis usually perpendicular to long axis of body. Sporogony unknown.

Fig. 184.—H. rara. (*After Laveran and Mesnil.*)

H. rara Laveran and Mesnil, 1902 (Fig. 184). In *Damonia reevesii* (Gray). Sporont club-shaped, 15 μ long by 2-3 μ wide, characterised by a greatly elongated cylindrical nucleus which occupies as a rule two-thirds of the length of the parasite. Schizogony and sporogony unknown.

H. mauritanica Sergent, 1904. In Algerian tortoise, *Testudo ibera* (Pall) (= *T. mauritanica* D. and B.). Schizogony in liver. Cytocysts contain eight sausage-shaped merozoites 8 μ long by 2 μ broad. Sporonts in thick capsule 12-15 μ long by 6 μ wide. Sporogony according to Papovici Baznosanu in a tick *Hyalomma syriacum* Koch (= *H. affine* Neum.).

H. bagensis Ducloux, 1904. In *Clemmys leprosa* (Schweigg). Sporogony, according to Brumpt, in *Placobdella catenigera* (Moq.-Tand.). Oökinete with nucleus and blepharoplast.

H. nicoriæ Castellani and Willey, 1904. In *Nicoria trijuga* (Schweigg). Encapsuled sporont bean-shaped, 10 μ long. Schizogony and sporogony unknown.

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Other species, but not described or named, have been found by Danilewsky in *Testudo marginata* (Schoepff.), and in

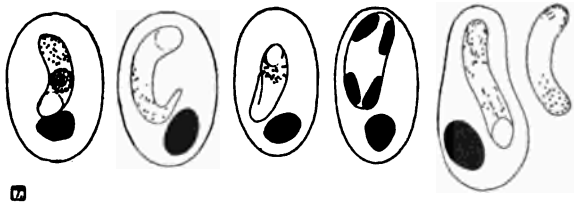

Fig. 185.—H. nicoriæ. (*After Castellani and Willey.*)

Trionyx sp.; by Lühe in *Dermatemys mawii* Gray, in *Cyclemys trifasciata* (Bell), and in *Sternothærus* sp. (Fig. 185).

C.—OPHIDIA.

H. pythonis (Billet, 1895) (=*Danilewskya pythonis*). In erythrocytes of reticulated python, *Python reticulatus* (Schn.).

Fig. 186.—H. pococki. (*After Sambon and Seligmann.*)

H. pococki Sambon and Seligmann, 1907 (Fig. 186). In Indian python, *Python molurus* (L.). Encysted sporont bean-shaped 14-16 μ long. Schizogony and sporogony unknown. Host-cell unaltered. Nucleus displaced.

Fig. 187.—H. shattocki. (*After Sambon and Seligmann.*)

H. shattocki Sambon and Seligmann, 1907 (Fig. 187). In diamond snake, *Python spilotes* (Lacép.). Encysted sporonts 22 μ long by 4 μ broad. Nucleus median. Host-cell sometimes slightly distorted. Schizogony and sporogony unknown.

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H. mirabilis Castellani and Willey, 1904 (Fig. 188). In *Tropidonotus piscator* (Schn.). Encysted sporont 12 μ long,

Fig. 188.—H. mirabilis. (*After Castellani and Willey.*)

capsule stippled with red dots when deeply stained by Romanowsky's method.

H. najæ Laveran, 1902. In the Indian cobra, *Naja tripudians* (Merr.). Sporont encapsuled 14 μ long, outstretched 21-22 μ long by 3 μ broad at anterior extremity. Host-cell slightly enlarged, nucleus displaced. Schizogony and sporogony unknown.

H. mocassini Laveran, 1902. In *Ancistrodon piscivorus* (Pal.). Sporont encysted 12-17 μ long, outstretched 20-25 μ. Host-cell elongated, nucleus displaced, flattened, sometimes hypertrophied. Schizogony and sporogony unknown.

H. crotali Laveran, 1902. In a rattlesnake, *Crotalus confluentus*. Sporont 15-16 μ by 5-6 μ. Host-cell destroyed. Its nucleus, considerably enlarged and elongated, may attain 16-18 μ in length. After disruption of erythrocyte, the nucleus of the host-cell remains as a rule adherent to encysted parasite.

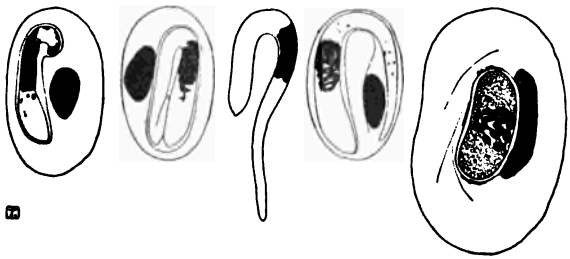

Fig. 189.—H. seligmanni. (*After Sambon.*)

H. seligmanni Sambon, 1907 (Fig. 189). In erythrocytes of bushmaster, *Lachesis mutus*. Fully grown doubled-up sporont within capsule 16 μ long by 6 μ wide. Outstretched parasite 41 μ long by 3·5 μ broad at anterior extremity. Nucleus median 5-6 μ long. Host-cell little altered; nucleus displaced. Other large encapsuled forms, 18 μ long by 7 μ broad, with cytoplasm more deeply staining, occur in greatly enlarged and attenuated cells with nucleus hypertrophied and adherent to capsule. Schizogony and sporogony unknown.

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H. zamenis Laveran, 1902. In horse-shoe snake, *Zamenis hippocrepis* L.

Fig. 190.—H. mansoni. (*After Sambon and Seligmann.*)

H. mansoni Sambon and Seligmann, 1907 (Fig. 190). In testaceous snake, *Zamenis flagelliformis* L. Sporont within capsule 12-13 μ long by 5-6 μ broad. Free form 17-23 μ long by 3-5 μ broad. Schizogony and sporogony unknown.

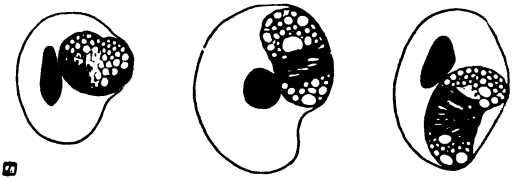

Fig. 191.—H. refringens. (*After Sambon and Seligmann.*)

H. refringens Sambon and Seligmann, 1907 (Fig. 191). In hoary snake, *Pseudaspis cana* (L.). Sporonts in oval or bean-shaped cysts 10-12 μ long by 5-6 μ in width. Cytoplasm literally crammed with rounded highly refractive granules.

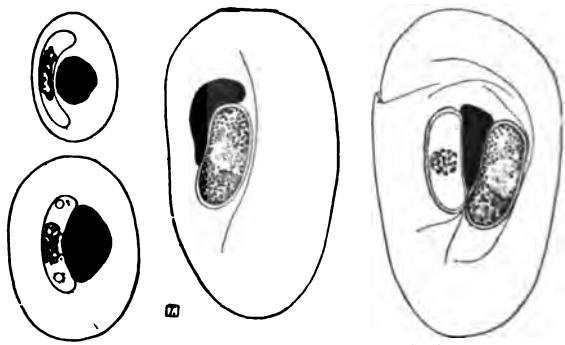

Fig. 192.—H. rarefaciens. (*After Sambon and Seligmann.*)

H. rarefaciens Sambon and Seligmann, 1907 (Fig. 192). In erythrocytes and leucocytes of Couper's snake, *Coluber corais*, var. *couperi*, Holbr. Sporonts sexually differentiated, doubled up and enclosed in bean-shaped capsules 12-13 μ long by 4-5 μ

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broad. Host-cell enlarged to about four times the normal size, entirely dehæmoglobinised and remarkably attenuated, nucleus hypertrophied.

H. viperina Billet, 1904, emend. In viperine snake, *Tropidonotus viperinus* Latr. in Algeria. Host-cell enlarged, dehæmoglobinised, becomes stippled with Schüffner's dots when deeply stained by Romanowsky's method; these red staining granules form concentric circles round the parasite-containing nucleus. The nucleus at first hypertrophied and deformed, ultimately almost entirely destroyed.

H. joannoni Hagenmüller, 1898. In *Macroprotodon cucullatus* (Geoffr.).

H. bungari Billet, 1895. In *Bungarus fasciatus* Schneid.

H. colubri Börner, 1901. In erythrocytes and leucocytes of *Coluber longissimus* Laur. (= *C. æsculapii* Host).

H. serpentium Lutz, 1901. In *Eunectes murinus* L. To the same species Lutz erroneously ascribes a number of Hæmogregarines found in *Boa constrictor*, *Drymobius bifossatus*, *Coluber corais*, *Spilotes pullatus*, *Xenodon newiedii*, *Rhadinæa merremii*, *Philodryas olfersii*, *Herpetodryas carinata*, and in various species of *Crotalus* and *Bothrops*. Lutz found that the schizogony of some of the hæmogregarines of snakes occurs within the capillaries of the lungs. He observed both micro- and macromerozoites.

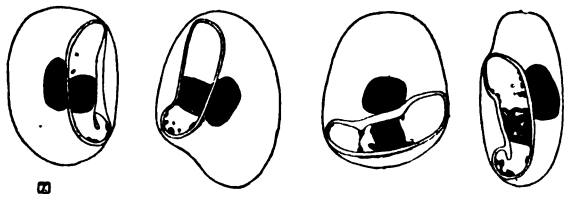

Fig. 193.—H. cantliei. (*After Sambon.*)

H. cantliei Sambon, 1907. In conical eryx, *Eryx conicus*. Encapsuled sporont 15-16 μ by 4·5-5 μ. Free form 15 μ long by 3·5 broad. Schizogony and sporogony unknown. (Fig. 193.)

Fig. 194.—H. terzii. (*After Sambon and Seligmann.*)

H. terzii Sambon and Seligmann, 1907. In common boa, *Boa constrictor*. Encapsuled sporont 11-14 μ long by 3-3·5 μ broad. Schizogony and sporogony unknown. (Fig. 194.)

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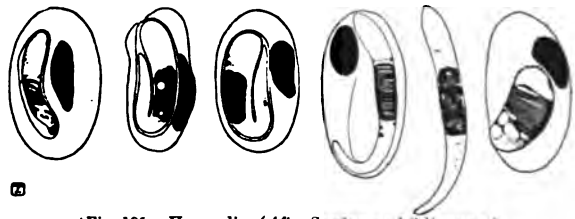

Fig. 195.—H. wardi. (*After Sambon and Seligmann.*)

H. wardi Sambon and Seligmann, 1907. In king snake, *Coronella getula*. Fully grown encapsuled sporonts 13-17 μ long by 4·5-5·5 μ broad. Free form 30-32 μ long by 2·8-3·5 μ broad. Schizogony and sporogony unknown. (Fig. 195.)

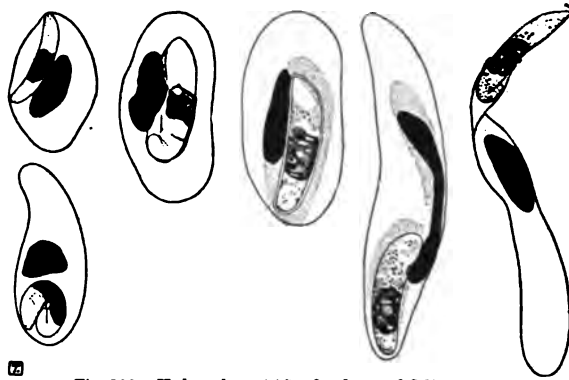

Fig. 196.—H. brendæ. (*After Sambon and Seligmann.*)

H. brendæ Sambon and Seligmann, 1907. In hissing sand snake, *Psammophis sibilans*. Encapsuled sporont 16-17 μ long by 4-4·5 μ broad. Host-cell greatly enlarged, especially in the long diameter. Schizogony and sporogony unknown. (Fig. 196.)

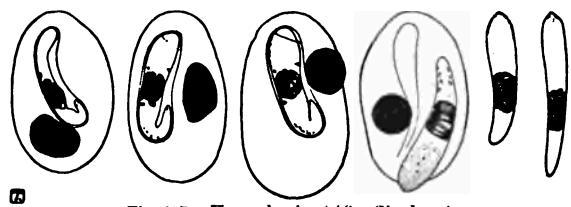

Fig. 197.—H. samboni. (*After Giordano.*)

H. samboni Giordano, 1907. In the black viper, *Vipera*

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aspis (L.). Encapsuled sporont 13-15 μ long by 3·5-4·5 μ broad. Free form 17-21 μ by 2·8-4 μ. Schizogony and sporogony unknown. (Fig. 197.)

H. lühei Sambon, 1907. In Cook's tree boa, *Corellas cooki*. Fully grown encapsuled sporont 12-14 μ long by 4-6 μ broad. Schizogony and sporogony unknown.

H. brumpti Sambon, 1907. In Mexican snake. Encapsuled sporont 14-17 μ long by 4·5-5 μ broad. Schizogony and sporogony unknown.

D.—SAURIA.

H. lacertarum (Danielewsky, 1885) (=*Karyolysus lacertarum* Labbé), Fig. 198. In the erythrocytes of the wall lizard,

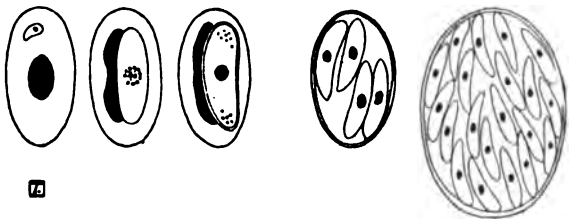

Fig. 198.—H. lacertarum.

Lacerta muralis Laur., and in *L. viridis* Laur., *L. agilis* L., and *L. ocellata* Daud. Schizogony in spleen, liver or kidney. Cytocyst oval, rarely round, 14-30 μ, enclosing either few (4-5) or many (20-25) macromerozoites (12 $\mu \times$ 3-4 μ), or, more rarely (in summer), numerous micromerozoites (8 $\mu \times$ 2 μ). Sporont 15 μ long by 5-6 μ broad. Two forms presenting indications of sexual differentiation. Forms with deeply staining granular cytoplasm often present unstainable light refracting granules at one or both extremities, or near the nucleus, which is seldom clearly visible. Host-cell considerably hypertrophied and dehæmoglobinised, nucleus elongated, misshapen and fragmented. Sporogony, according to Schaudinn, in *Ixodes ricinus* (L.). The larvæ and nymphæ of this tick live on lizards, and Schaudinn proved that they may transmit the infection not only directly, but also through their progeny —a necessary provision, because during the adult stage they attack mammals only.

H. platydactyli Billet, 1900. In the Moorish gecko, *Tarantula mauritanica* (L.) (=*Platydactylus mauritanicus*).

H. mabuiæ Nicolle and Comte, 1906. In *Mabuia vittata* Olivier.

H. varani Laveran, 1905. In *Varanus niloticus* L., at Pretoria.

H. sergentium Nicolle, 1904. In *Chalcides ocellatus* (Forsk) (=*Gongylus ocellatus*).

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H. biretorta Nicolle, 1904. In *Lacerta ocellata* Daud.

H. Psammodromi (Soulié, 1904) (= *Karyolysus psammodromi*). In *Psammodromus algirus* (L.), Algeria.

H. curvirostris Billet, 1904. In *Lacerta ocellata* Daud.

H. lacazei Labbé, 1894. In *Lacerta muralis* Laur. and *L. agilis* L.

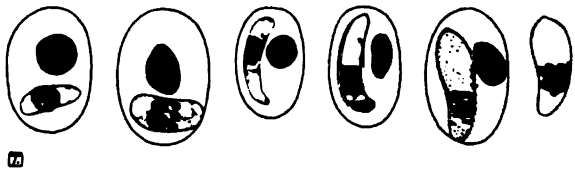

Fig. 199.—H. erlichi. (*After Sambon.*)

H. erlichi Sambon, 1907. In *Varanus exanthematicus*. Encapsuled sporont 11-14 μ long by 3·5-4·5 μ broad. Free form 12 μ by 4 μ. Schizogony and sporogony unknown. (Fig. 199.)

Other hæmogregarines not described or named have been found in *Varanus dracena* and *V. arenarius*.

HÆMOGREGARINES OF AMPHIBIANS.

H. tritonis (Fantham, 1905) (= *Lankestrella tritonis*). In *Molge cristata* (Laur.) (= *Triton cristatus*). Parasite varies in size from 2 to 6 μ. Mature schizont breaks up into 8 or 9 merozoites.

H. riedyi. In a Californian salamander, *Batrachoseps attenuatus*.

H. minima (Chaussat) (= *Anguillula minima* Chaussat, *Drepanidium ranarum* Lankester, *Lacerania ranarum* Grassi, *Hæmogregarina ranarum* Kruse e.p., *Drepanidium princeps* Labbé, *Lankestrella ranarum* Labbé, *Dactylosoma splendens* Labbé, *Drepanidium monilis* Labbé). In the edible frog, *Rana esculenta* L. In erythrocytes, leucocytes or tissue cells. Schizogony in spleen, liver, and more rarely in kidneys and bone marrow. Cytocysts round, 28-30 μ, with 5, 6 or 8 macromerozoites 5-8 μ long, or more numerous micromerozoites, 3-4 μ, especially in summer. Sporont club-shaped, 12-15 μ long; nucleus central; two bright spots, one on each side of nucleus. Host-cell apparently unaltered. Sporogony, according to Billet, takes place in a leech of the genus *Helobdella*. In examining a number of leeches which had been sucking the blood of frogs infected with hæmogregarines, he found in the intestine a trypanosome, *Trypanosoma inopinatum*, and other forms intermediate between a hæmogregarine and a trypanosome. Some of the frogs had in their blood both *Hæmogregarina minima* and *Trypanosoma inopinatum*, whilst others had only the hæmogregarine; nevertheless the leech in both instances presented trypanosomes. Subsequently Billet

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placed leeches whose digestive tube contained *T. inopinatum* on frogs free from hæmoprotozoa: afterwards he found hæmogregarines only in these frogs. Billet considers the trypanosome phase to be very uncommon in the frog, but of general occurrence in the leech, and, conversely, the hæmogregarine phase to be absent, as such, in the invertebrate host, but common in the vertebrate.

H. magna (Grassi and Feletti) (= *H. ranarum* Kruse, e.p., *Drepanidium magnum* Grassi and Feletti, *D. Krusei* Labbé, *Danilewskya Krusei* Labbé, *Hæmogregarina magna* Labbé). In *Rana esculenta* L.

H. tunisiensis Nicolle, 1904. In Algerian toad, *Bufo mauritanicus* Schleg. Sporont club-shaped and doubled up in capsule, 12-15 μ by 8 μ. Capsule formed of two coats; the inner one presents Schüffner's dots when stained by Romanowsky's method.

H. theileri Laveran, 1905. In *Rana angolensis* Bocage. Sporont 24 μ long by 4 μ broad at anterior extremity, doubled up in capsule 15-17 μ long by 5-6 μ broad. Host-cell enlarged, dehæmoglobinised, nucleus fragmented.

H. neireti Laveran, 1905. In *Rana mascareniensis* D. and B. Sporont doubled up in oval capsule 16-21 μ long by 11-14 μ

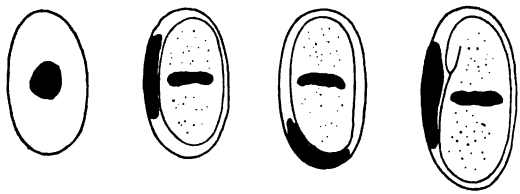

Fig. 200.—H. neireti. (*After Laveran.*)

broad. Nucleus elongated in the direction of the short axis of the parasite. Host-cell considerably enlarged. (Fig. 200.)

H. clamatæ Stebbins. In *Rana clamata.*

H. castebianæ Stebbins. In *Rana castebiana.*

H. berestnieffi Castillain and Willey, 1904. Found by Berestnieff in *Rana tigrina.*

Berestnieff ascribes to the last-named species another hæmogregarine found in *Rana limnocharis* Bori.

Other hæmogregarines have been found by Brumpt in an Abyssinian toad near Immi, and by Durham in a toad at Para, Brazil. The sporogony of the latter seems to occur in ticks. Durham found in ticks which had fed on infected toads appearances suggestive of conjugation of the parasite, in addition to oöcysts up to 60 μ in diameter.

Hæmogregarines of Fish.

H. bigemina Laveran and Mesnil, 1901 (Fig. 201). In the

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shanny or smooth blenny, *Blennius pholis* L., and in *B. montagui*. Schizogony in erythrocytes by binary fission.

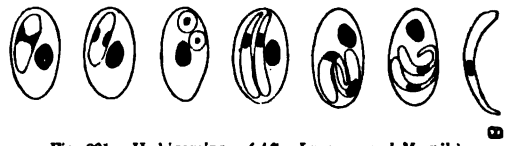

Fig. 201.—H. bigemina. (*After Laveran and Mesnil.*)

H. quadrigemina (Brumpt and Lebailly, 1904) (= *H. callionymi*, Br. and Leb.), Fig. 202. In *Callionymus lyra*.

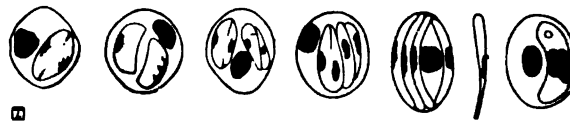

Fig. 202.—H. quadrigemina. (*After Brumpt and Lebailly.*)

Schizogony in erythrocytes by longitudinal division into four merozoites.

H. simondi Laveran and Mesnil, 1901 (Fig. 203). In the sole, *Solea vulgaris*. Schizont 19-20 μ long, 2 μ broad, club-shaped, nucleus median or nearer anterior extremity. Schizogony in erythrocytes in peripheral blood. Mature

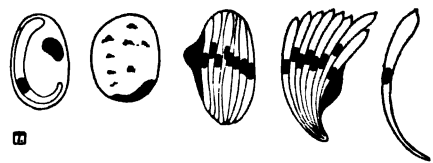

Fig. 203.—H. simondi. (*After Brumpt and Lebailly.*)

schizont becomes globular, occupying entirely the enlarged host-cell, of which only the nucleus remains. Cytocyst encloses 2, 4 or 8 merozoites. Sporogony possibly in *Platybdella solex* (Kröyer), a leech frequently found on soles. Brumpt found in this leech oökinetes similar to those seen in *Placobdella catenigera*. (See *Hæmogregarina bagensis*, p. 815.)

H. platessæ Lebailly, 1904. In the plaice, *Pleuronectes platessa* (L.).

H. flesi Lebailly, 1904. In common flounder, *Pleuronectus flesus* (L.).

H. laternæ Lebailly, 1904. In *Arnoglossus laterna* (Walb.) (= *Platophrys laterna*).

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H. cotti Brumpt and Lebailly, 1904. In *Cottus bubalis* Euphr.

H. blanchardi Brumpt and Lebailly, 1904 (= *H. gobii* Brumpt and Lebailly).

H. bothi Lebailly, 1905. In brill, *Bothus rhombus*.

H. delagei Laveran and Mesnil, 1902. In two skates, *Raja punctata* Risso, and *R. mosaica* Lacép.

H. lignieresi Laveran, 1906. In eel at Buenos Ayres.

2. Plasmodidæ. Lühe, 1906.

Synonyms.—*Gymnosporidia* Labbé, 1894; *Acystosporidia* von Wasielewski, 1896; *Hæmamœbidæ* Ross, 1899; *Acystosporea*, Minchin, 1903.

Schizont epicellular or endocellular (in erythrocytes) during the whole period of growth; always more or less actively amœboid; produces hæmozoin. *Schizogony* by multiple segmentation (rosette formation). *Merozoites* rounded or ovoid at the time of segmentation, more or less elongated when free in the plasma; never flagellate. *Sporonts* endocellular; round or crescentic when full grown; sexual differentiation marked. *Sporogony* in *Culicidæ; oökinete* encysts in the wall of mosquito's stomach, increases greatly in volume, and divides into a number of daughter cells which produce on their surface numerous elongated *sporozoites*. Emptied into the body cavity of the insect, through the bursting of the enclosing cyst, the sporozoites reach the salivary glands and pass with the saliva into the blood of the vertebrate intermediary host while the mosquito is feeding.

Two genera:

(1) *Plasmodium*.

(2) *Laverania*.

(1) Plasmodium. Marchiafava and Celli, 1885.

Synonyms.—*Oscillaria* Laveran, 1881; *Hæmatomonas* Osler, 1887; *Hæmatophyllum* Metchnikoff, 1887; *Hæmamœba* Grassi and Feletti, 1889; *Laverania* Grassi and Feletti, 1889; *Cytamœba* Danilewsky, 1890; *Proteosoma* Labbé, 1894; *Hæmosporidium* Lewkowicz, 1897; *Cytosporon* von Wasielewski, 1901.

Gametocytes round.

Type species, *P. vivax*.

SPECIES DETERMINED:

P. vivax (Grassi and Feletti, 1890) (= *Hæmamœba vivax* Grassi and Feletti, *H. malariæ* var. *magna* Lav. 1900 e.p., *H. malariæ* var. *tertianæ* Lav. 1901, *Plasmodium malariæ* var. *tertianæ* Celli and Sanf., 1891, *P. malariæ tertianum* Labbé, 1899, *Hæmosporidium tertianum* Lewkowicz, 1897), Fig. 204. Parasite of tertian fever in man. Full-grown schizont about 10 μ in diameter, nucleus at periphery, hæmozoin in fine reddish

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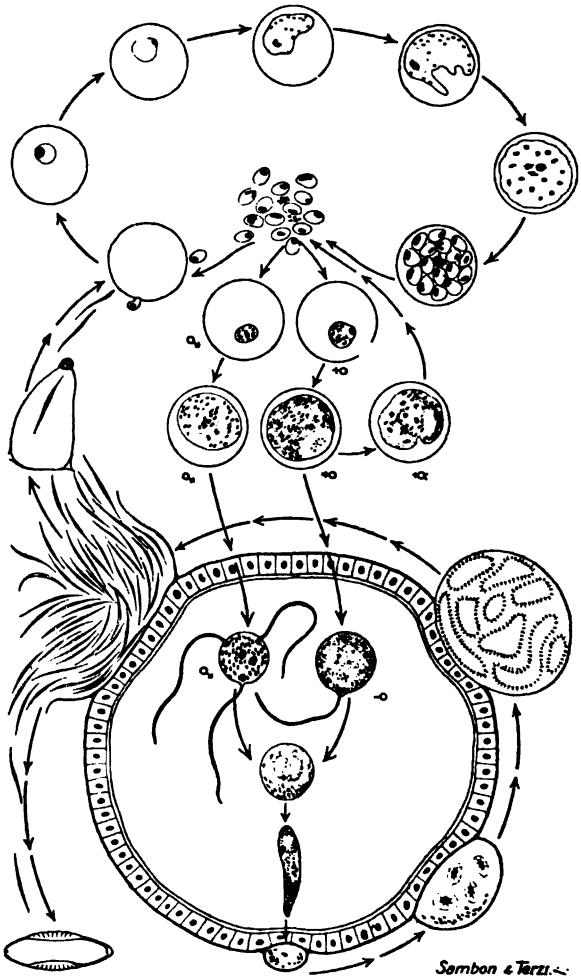

Fig. 204.--Plasmodium vivax: schema of entire life cycle.

granules. Schizogony in peripheral circulation, endocorpuscular cycle 48 hours; merozoites 14 to 20, rarely 22 or 24. Early forms actively amœboid. Host-cell greatly swollen and decolorised; in stained specimens presents peculiar stippling

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Schüffner's dots. Gametocytes 12 to 16 μ; hæmozoin in coarse granules, sometimes rod-shaped. Sporogony in various species of *Anophelinæ*.

P. malariæ (Laveran, 1881, *sensu stricto*) (= *Hæmamœba malariæ* Grassi and Feletti, 1890, *pro parte*, *H. laverani* var. *quartana* Labbé, 1894; *H. malariæ* var. *magna* Lav., 1900 e.p.; *H. malariæ* var. *quartanæ* Lav. 1901; *Plasmodium malariæ* var. *quartanæ* Celli and Sanf., 1891; *P. malariæ quartanum* Labbé, 1899; *Hæmosporidium quartanæ* Lewkowicz, 1897; *P. golgii* Sambon, 1902; *Laverania malariæ* Janeso, 1905), parasite of quartan fever in man. Full-grown schizont somewhat smaller than a normal erythrocyte, hæmozoin granules coarser and darker than in *P. vivax*. Schizogony in peripheral circulation; endocorpuscular cycle 72 hours: merozoites 6 to 12 or 14. Early forms show a sharper outline than those of *P. vivax*, their amœboid movements are slower and less marked. Host-cell becomes a trifle smaller and darker than the normal erythrocytes. Gametocytes scarce and of various sizes. Some smaller than a normal erythrocyte, others twice this size. Sporogony in various species of *Anophelinæ*.

Fig. 205.—P. kochi. (*After Lühe.*)

P. kochi (Laveran, 1899) (= *Hæmamœba kochi* Lav., 1889), Fig. 205. In *Cercopithecus sabacus* and other African guenons. Schizogony not observed. Early ring-like forms and sporonts somewhat similar to those of *P. vivax*. Host-cell apparently little altered. Sporogony unknown.

P. pitheci Halberstædter and Prowazek, 1907. In the ourang-outang, *Simia satyrus* L. Schizogony as in *P. vivax*: hæmozoin granules coarse, rod-shaped. Infected apes showed no signs of illness, their temperature varied from 37·5° to 38·3° C. Inoculation of infected blood reproduced the disease in normal ourang-outangs, but was negative in gibbons and lower apes.

A similar parasite has been found by Ziemann and Lühe in the chimpanzee, *Anthropopithecus troglodytes* (Gm.).

P. cynomolgi Mayer, 1907, in blood of *Macacus cynomolgus* (L.)., Java. Schizogony in peripheral blood. Merozoites 8-13. Gametocytes similar to those of *P. vivax*, but smaller. Host-cell presents Schüffner's dots when stained by Romanowsky's method. Sporogony unknown.

P. inui Halberstædter and Prowazek, 1907. In Macaque monkey, *Macacus cynomolgus* L., and in the pig-tailed monkey, *M. nemestrinus* (L.); characterised by fine yellow hæmozoin granules. Schizogony in peripheral blood; merozoites 12 to

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16. Host-cell does not present Schüffner's dots. Sporogony unknown.

Other similar parasites have been found by Kossel in the yellow baboon, *Cynocephalus babuinus* Desm., and by Dutton, Todd and Tobey in other undetermined monkeys.

P. melanipherum (Dionisi, 1898) (= *Polychromophilus melanipherus* Dionisi, 1898; *Hæmamœba melaniphera* Lav., 1899), Fig. 206. Found by Dionisi in *Miniopterus schreibersii*,

Fig. 206.—P. melanipherum.

by Sambon and Low in the hairy-tail bat, *Myotis capaccinii*. Gametocytes ovoid or roundish; hæmozoin in coarse black granules. Host-cell somewhat altered in shape, but not appreciably enlarged. Schizogony, according to Schingareff, in capillaries of liver; 20-22 merozoites. Sporogony unknown. The *Nycteribiidæ* have been suggested as possible alternative hosts.

P. murinum (Dionisi, 1898) (= *Polychromophilus murinus* Dionisi, 1898). In *Myotis myotis*, gametocytes ovoid. Early forms ring-shaped or oval. Frequently two oval forms in the same erythrocyte. Host-cell distorted and dehæmoglobinised. Sporogony unknown. The same species (?) is reported by Bowhill in *Vespertilio capensis* and by Schingareff in *V. daubentoni*.

P. monosoma Vassal, 1907. In *Vesperugo abramus* (?) Schizogony unknown. Gametocytes 8·5 μ to 9 μ in diameter. Sporogony unknown.

Fig. 207.—P. vassali.

P. vassali Sambon, 1907 (Fig. 207). In a squirrel, *Sciurus griseimanus*. Schizogony unknown. Gametocytes round or ovoid, 7 to 8 μ. Host-cell not appreciably altered. Sporogony unknown.

P. danilewskyi (Grassi and Feletti, 1890) (= *Laverania danilewsky* Grassi and Feletti, 1890; *Hæmamœba relicta* Grassi and Feletti, 1891; *Cytosporon malariæ avium* Danilewsky, 1891; *Proteosoma grassii* Labbé, 1894; *Plasmodium relictum* Sergent, 1907). In erythrocytes of *Passer domesticus*. Sporogony in various species of *Culicinæ*. To this species have been erroneously ascribed numerous hæmoprotozoa of birds belonging not only to different species, but also to different families.

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P. vaughani Novy and McNeal, 1904. In *Merula migratoria*. Sporogony unknown.

P. simondi (Castellani and Willey, 1904) (= *Hæmocystidum simondi*), Fig. 208. In erythrocytes of a tree-dwelling gecko,

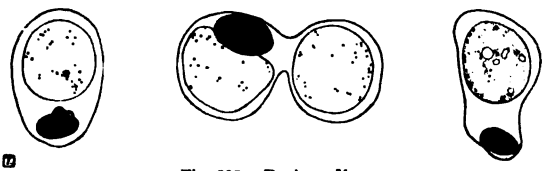

Fig. 208.—P. simondi.

Hemidactylus leschenaulti, in Ceylon. Schizogony unknown. Only gametocytes observed. Sporogony unknown.

(2) LAVERANIA. GRASSI AND FELETTI, 1889.

Synonyms.—*Hæmomenas* Ross, 1899; also synonyms mentioned with genus *Plasmodium*.

Gametocytes crescentic.

Type species, *L. malariæ*.

SPECIES DETERMINED:

L. malariæ (Grassi and Feletti, 1890) (= *Hæmamœba malariæ parva* Lav., 1900; *H. præcox* Grassi and Feletti, 1890 e.p.; *H. laverani* Labbé, 1894; *Plasmodium malariæ* var. *quotidianæ* Celli and Sanf, 1891; *P. præcox* Doflein, 1901; *P. immaculatum* Schaud, 1902; *P. falciparum* Blanchard, 1905; *Hæmomenas præcox* Ross, 1899; *Hæmosporidium undecimanæ* + *H. sedecimanæ* + *H. vigesimo-tertianæ* + *H. spec.* Lewkowicz, 1897; *Hæmatozoön falciparum* Welch, 1897; *H. immaculata* Grassi and Feletti, 1891 e.p.), Fig. 209. Para-

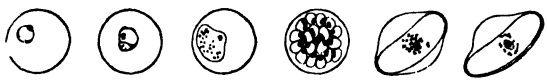

Fig. 209.—L. malariæ.

site of subtertian fever in man. Full-grown schizont rarely attains half the size of normal erythrocyte, hæmozoin in very fine granules. Schizogony takes place within the internal organs (spleen, bone marrow); endocorpuscular cycle about 48 hours; merozoites usually 14 to 16, sometimes 20 or even 30. Host-cell sometimes shrunken, and of a deeper, somewhat greenish colour. Gametocytes measure about 9 to 12 μ in length by 2 to 3 μ in width. Sporogony in various species of *Anophelinæ*.

Two species reported to be causes of true quotidian

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intermittent fever are assigned to the genus Laverania, but there is much uncertainty about these organisms. One species (*L. præcox*) is stated to produce hæmozoin during the period of its growth, the other (*L. immaculata*) not, but the crescentic gametocytes ascribed to both are said to contain numerous granules of hæmozoin. These parasites probably have been confounded with those of *L. malariæ*, with which they are said to be usually associated.

3. Spiroschaudinniidæ. Sambon, 1907.

Under the term *Spiroschaudinniidæ* are here provisionally grouped the following three genera :—

(1) *Leucocytozoön.*
(2) *Spiroschaudinnia.*
(3) *Treponema.*

(1). Leucocytozoön.* Danilewsky, 1889.

Synonyms.—*Hæmamœba* Laveran, 1903 ; *Spirochæte* Schaudinn, 1904 ; *Trypanomorpha* Léger, 1906.

Schizont alternately free in plasma and endocellular (in erythroblasts). Free form resembles in structure a minute slender trypanosome with nucleus, blepharoplast, undulating membrane and flagellum. Endocellular form discards locomotor apparatus and becomes amœboid. It does not produce hæmozoin. *Schizogony* takes place during free phase by longitudinal fission. The resulting division forms may remain coherent by their anterior extremities and accordingly move in either direction. Further division frequently takes place while the individuals of a couple continue to cohere. Under unfavourable conditions the free schizonts agglomerate into irregular clumps. *Sporonts* attain a comparatively large size and present sexual differentiation. In the free phase during growth they develop a flagellum and a broad undulating membrane. The flagellum ends with the undulating membrane at the posterior extremity of the body in the ♀, but extends freely beyond in the ♂. There are sixteen myonemes (muscle-fibrillæ) in each gametocyte, but in the ♂ they are arranged in four double pairs on each side (Fig. 210). When fully grown the sporonts encyst. They shed their locomotor apparatus and appear as large spherical or oval bodies enclosed within an oval or spindle-shaped capsule composed of their own periplast and the

* The gametocytes of the Leucocytozoa were first described by Danilewsky in 1889, but nothing was known of the life history of these parasites until 1904, when Schaudinn published his remarkable paper on the development of *L. ziemanni*. The accuracy of Schaudinn's observations has been disputed by Novy and MacNeal, who believe he confounded various kinds of protozoal parasites owing to the multiple infection of both his owls and mosquitoes.

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remains of the host-cell and its nucleus.* *Sporogony* so far as known in *Culicidæ*. In insect's stomach the gametocytes burst out of their cysts and the microgametocytes give rise to eight microgametes provided with undulating membrane while the residual body breaks up into two or three parts. *Oökinete* does not encyst, but increases considerably in length, coils itself into a compact mass, and by a process of segmentation subsequent to successive divisions of its nucleus, gives rise to numerous sporozoites which, after separating from the coil, elongate and closely resemble the filiform schizonts. According to the nature of the oökinete from which they originate, the sporozoites are either indifferent, male or female. On swarming out of the oökinete skeins, the sporozoites multiply by rapid successive divisions; the ultimate division forms become so minute that they are only discernible when agglomerated. When digestion of the blood-feed is completed in the mosquito the sporozoites migrate to the malpighian tubes and go through a period of rest in the cells lining these organs, loosing their locomotor apparatus, but retaining the two chromatine bodies and becoming pear-shaped. When the mosquito next feeds the sporozoites are swept back into the intestine with the shed epithelium. They then leave their host-cells, pierce the walls of the gut, and finally reach the pharynx of the insect to pass into the avian host on which the mosquito is feeding.

Type species, *L. ziemanni*.

SPECIES DETERMINED:

L. ziemanni (Laveran, 1903) (= *Hæmamœba ziemanni*), Fig. 210. Schizogony in erythroblasts of the naked-footed owlet,

* To explain the presence of a cell-nucleus between the body of the full-grown gametocyte and the enveloping element which he believes to be the cast-off periplast from which the parasite has contracted, Schaudinn suggests that when the sporonts become too large to re-enter the erythroblasts they engulf the latter instead. Dutton, Todd, and Tobey have likewise seen erythrocytes engulfed by *Typanosoma notatorium*. According to Danilewsky, Sacharoff, Ziemann and Berestneff, the element enclosing the gametocytes is a leucocyte. Laveran believes it to be an erythrocyte. He describes as such the element enclosing the gametocytes of *L. smithi*, and mentions a fact, namely, the occurrence of *two parasites within the same host-cell*, which is certainly opposed to Schaudinn's surmise. The action of the parasite on the host cell and its nucleus seems to vary in different species of Leucocytozoa. Some appear to exert no action on the nucleus, others enlarge it, flatten it, fragment it, or destroy it entirely. The occasional absence of the nucleus has no significance. The host-cell nucleus is not infrequently extruded from erythrocytes of birds enclosing hæmoproteidæ, or from the red cells of reptiles containing hæmogregarinidæ. The sporonts of *Hæmogregarina brendæ* bring about a characteristic elongation and dehæmoglobinisation of the affected erythrocytes, which seems most suggestive towards the interpretation of the peculiar elongated elements enclosing the Leucocytozoön gametes.

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Glaucidium noctuæ (Retz.). Sporogony, according to Schaudinn, in *Culex pipiens* L.

To this species is ascribed a parasite found by Laveran in the wood-owl, *Syrnicum aluco* L.

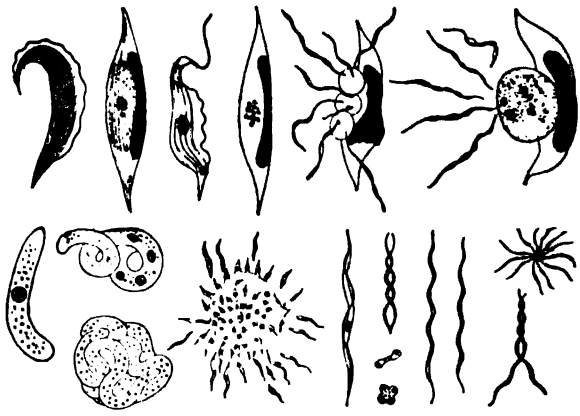

Fig. 210.—Different stages in the development of L. ziemanni. (*After Schaudinn.*)

L. smithi (Laveran and Lucet, 1905) (=*Hæmamœbi smithi*). Sporonts in erythrocytes of domesticated turkey, *Meleagris gallo-pavo domestica* L. Schizogony not observed. Sporogony unknown.

L. neavei (Balfour, 1906) (=*Hæmamœbi neavei*). Sporonts in blood of Abyssinian guinea-fowl, *Numida ptilorhyncha* Licht. Schizogony not observed. Sporogony unknown. (Fig. 211.)

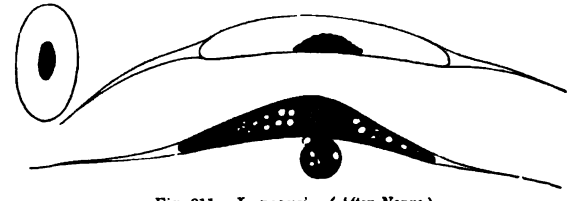

Fig. 211.—L. neavei. (*After Neave.*)

L. toddi Sambon, 1907. Sporonts in blood of a Congo grey hawk, *Asturinula monogrammica*. Schizogony not observed. Sporogony unknown.

L. lovati Seligmann and Sambon, 1907. Sporonts in the blood of the red grouse, *Lagopus scoticus* (Lath.). Schizogony not observed. Sporogony unknown.

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Similar parasites have been found by Sacharoff and Berestneff in the blood of crows, rooks and magpies.

(2) SPIROSCHAUDINNIA. SAMBON, 1907.

Synonyms. — *Spirochæta* Ehrenberg, 1843, *pro parte; Spirochæte* Cohn, 1875, *pro parte.*

The name *Spiroschaudinnia* is here proposed to designate an important group of blood parasites hitherto referred to the genus *Spirochæta.* *S. recurrentis*, type species of the new genus, differs considerably both in structure and life history from the free-living organism to which Ehrenberg applied the name *Spirochæta.* Unfortunately our knowledge of the Spiroschaudinniæ is very imperfect, and their biological position is a matter of controversy. The majority of observers believe them to be bacteria, asserting that they multiply by transverse division, that they possess numerous flagella, and that they are plasmolysed by solutions of NaCl and alkalies. Others contend that they are protozoa, that they multiply by longitudinal division, have no flagella, are not plasmolysed by solutions of NaCl and alkalies, and do not grow on ordinary culture media. These conflicting statements are certainly perplexing, but the question is not so important as it appears, the differentials being totally arbitrary. We place the Spiroschaudinniæ amongst the blood protozoa because morphologically they appear to be allied to the Leucocytozoa, and because their life history and pathogeny conform in a striking way with those of other hæmoprotozoa.

In the blood of the vertebrate host, the *schizonts* are minute, wavy or spirally twisted thread-like bodies of uniform length. According to Schaudinn and Prowazek they possess an undulating membrane, but no flagella. Their nuclear apparatus is composed of from six to eight chromatic granules arranged along an axial thread. *Schizogony* takes place by longitudinal division, but the resulting forms may remain attached end to end for some time, either twisted up together or placed in the same line. Sometimes more than two individuals are connected in this way, and their ultimate separation gives the impression of transverse division. The free phase alternates with an endocorpuscular resting phase which occurs within the internal organs of the host, the parasite coiling itself up within the host-cell. In the later stages of infection, relatively long, thick forms have been noticed; they may represent sporonts. *Sporogony* takes place in the *Ixodidæ.* The parasites have been found in great numbers within the ova of infected ticks, thus indicating that the infection may be transmitted by heredity.

SPECIES DETERMINED:

S. recurrentis (Lebert, 1874) (= *Spirochæta recurrentis* Lebert, 1874; *Spirochæta obermeyeri* Cohn, 1875). Cause of relapsing fever in man. Schizont 7 to 9 μ long by 0·25 to 0·3 μ broad. Sporogony probably in the common bed bug, *Acanthia lectularia* (L.).

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S. duttoni (Novy and Knapp, 1906). Cause of "tick fever" (relapsing fever) in Africa. Morphologically indistinguishable from *S. recurrentis*. Sporogony in *Ornithodoros moubata* (Murray).

S. anserina (Sacharoff, 1891). In blood of domestic goose, *Anser cinereus domesticus* Anct. Indistinguishable from *S. recurrentis*. Sporogony unknown.

S. gallinarum (R. Blanchard, 1905). Discoverod by Marchoux and Salimbeni. In domesticated fowls *Gallus gallinaceus* Pallas, in Brazil. Sporogony in *Argas miniatus* Koch.

S. theileri (Laveran, 1904). In blood of Transvaal oxen. Sporogony in the blue tick, *Margaropus decoloratus*.

S. ovina (R. Blanchard, 1906). Found by Martoglio and Carpano in the blood of Abyssinian sheep. Sporogony unknown.

S. jonesi Dutton, Todd and Tobey, 1906. In a Congo mud fish, *Clarias angolensis*, Steind. Length 18 μ; breadth at widest part 0·6 μ. Often in clusters. Sporogony unknown.

In addition to the above, spiroschaudinniæ have been found in the horse, bat, monkey, rat, mouse, bandicoot, and in various insects such as mosquitoes and tse-tse flies. The "disease of Miana" in Persia, known to be transmitted by *Argas persicus* Fisher, and other "tick diseases" in Central America and other tropical countries, are probably due to the inoculation of specific spiroschaudinniæ.

(3) TREPONEMA. SCHAUDINN, 1905.

Synonyms. — *Spirochæte* Schaudinn, 1905, *pro parte*, *Spironema* Vuillemin, 1905; *Microspironema* W. Stiles and Pfender, 1905.

Schizont minute thread-like body, with pointed tapering extremities and spirally twisted into numerous fine coils. No undulating membrane visible, but, according to Schaudinn, a flagellum at each extremity. *Schizogony* by longitudinal fission. The resulting division forms remain for a time connected by their ends (Cf. Leucocytozoön, spiroschaudinnia). *Sporogony* unknown. Krzysztalowicz and Siedlecki describe forms which they consider as sexually differentiated.

Type species *T. pallidum*.

SPECIES DETERMINED:

T. pallidum (Schaudinn, 1905) = *Spirochæta pallida* Schaudinn, 1905, *Spironema pallidum* Vuillemin, 1905, *Microspironema pallidum*, W. Stiles and Pfender, 1905, *Trypanosoma luis* Krzysztalowicz and Siedlecki, 1905. Cause of syphilis. Sporogony in an alternative invertebrate host appears to be entirely omitted in this species, transmission by direct inoculation of the schizogonic stage having become the ordinary method of propagation. An instructive analogy is that of dourine (horse syphilis) in which the pathogenic agent, a trypanosome, has likewise evolved a direct method of transmission. Malaria and other hæmoprotozoal diseases may be

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artificially transmitted by inoculation of the respective parasites in their schizogonic stage, and propagation in this manner may be continued indefinitely.

T. pertenuis (Castellani, 1905) = *Spirochæte pertenuis* Castellani, 1905, *S. pallidula* Castellani, 1905. Cause of yaws. Morphologically indistinguishable from *T. pallidum*. Sporogony unknown.

4. Hæmoproteidæ. Sambon, 1906.

Schizont alternately free and epi- or endocorpuscular. May or may not produce hæmozoin. *Schizogony* by longitudinal fission or multiple division. *Sporonts* free or endocellular when full grown, alternately free and epicellular or endocellular during growth. Free forms flagellate. *Oökinete* free. In accordance with inherited characters (smaller or larger nucleus, more or less chromatin, more or less reserve material) it develops into either an indifferent, or a female, or a male form. The indifferent forms multiply by longitudinal binary fission, and give rise to other indifferent forms, some of which may become sexually differentiated. Successive divisions reduce the size of the parasites. The minimal forms may be looked upon as homologous with the sporozoites of the encysted oökinetes of the Plasmodidæ. The male forms assume a round form and break up into eight microgametes. The female forms do not multiply at once, but become laden with reserve material and assume a resting condition between the epithelial cells of the host's mid-gut, losing all traces of the flagellum. After long periods, having gradually used up their reserve nutriment, they may revert to the indifferent type and reproduce indifferent forms by parthenogenesis.*

Two sub-families:

(A) *Hæmoproteinæ.*

(B) *Trypanosominæ.*

A. HÆMOPROTEINÆ.† SAMBON, 1906.

Synonyms.—*Halteridiidæ* (Neveu-Lemaire, 1901).

Schizont alternately free in plasma and endocorpuscular (erythrocytes). Endoglobular forms are amœboid and produce hæmozoin. Free forms flagellate. *Schizogony* by longitudinal division of free flagellate forms.‡ *Sporonts*, when full-grown, kidney-shaped and endocorpuscular; during period of growth, alternately free and endocellular. *Sporogony*

* Probably they are fertilised by the microgametes of the male forms before assuming the resting condition.

† The life history of the *Hæmoproteinæ* is here given as described by Schaudinn for *Hæmoproteus noctuæ*. Schaudinn's observations have been partially confirmed by Billet, Sergent and others. Novy and McNeal contend that they are erroneous.

‡ The endocorpuscular forms do not break up by multiple fission as suggested by earlier observers who confounded these parasites with concurrent Plasmodidæ.

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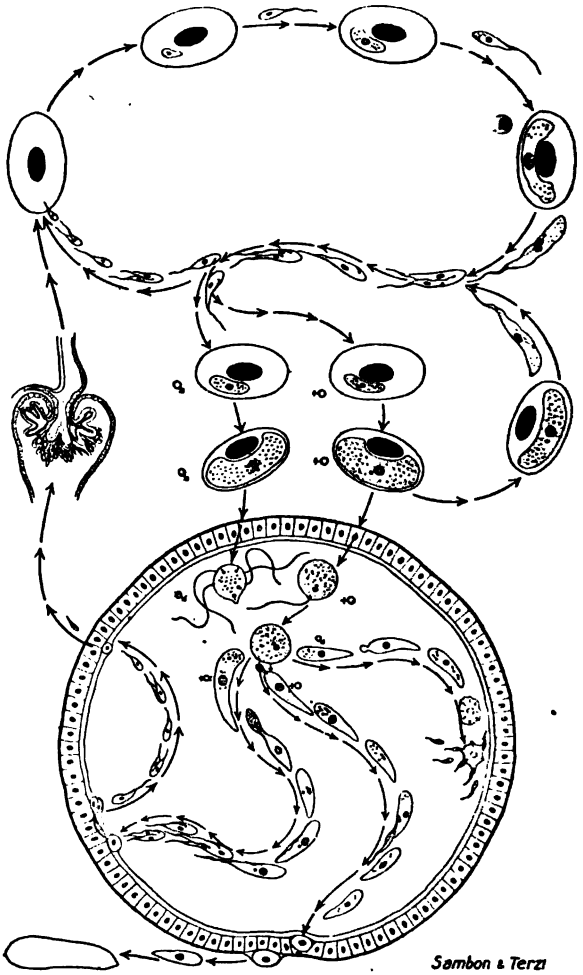

Fig. 212.—Entire life cycle of Hæmoproteus noctuæ, according to Schaudinn.

in Culicinæ or Hippoboscidæ. Microgametocyte gives rise to eight extremely slim fusiform microgametes provided with undulating membrane. Sporozoites, passing through the wall

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of the gut into the body cavity of the insect, form a thick cluster between the pumping organ and the pharyngeal valve; and by penetrating the tunica elastico-muscularis, which is very delicate at this part, pass into the pharynx and thence into the vertebrate host. Some of the parasites penetrate the ovaries of the insect host, and so passing through two generations of the latter, are finally inoculated by the offspring of the insect which originally took them up.

One genus:

Hæmoproteus.

Hæmoproteus. Kruse, 1890.

Synonyms. — *Halteridium* Labbé, 1894; *Laverania* Laveran, 1899; *Trypanosoma* Schaudinn, 1904; *Trypanomorpha* Léger, 1906.

Type species *H. noctuæ*.

SPECIES DETERMINED:

H. noctuæ (Celli and Sanfelice, 1891) (Fig. 212). In *Glaucidium noctua* (Retz). Sporogony in *Culex pipiens* (L.).

To the same species are ascribed other similar parasites found in the blood of *Strix flammea* (L.), *Scops gin* (Scop) and an "Algerian owl."

H. danilewskii (Kruse, 1890). In *Corvus cornix* (L.). Sporogony unknown.

H. columbæ (Celli and Sanfelice, 1891). In *Columba livia* (L.). Sporogony, according to Ed. and Et. Sergent, takes place in *Lynchia maura*, a fly belonging to the family Hippoboscidæ. The oökinete is club-shaped and measures 20-23 μ in length by 2·5-3 μ in breadth. The nucleus is median. The hæmozoin collected at the posterior extremity. Further stages of development in the fly were not observed, but the authors claim to have obtained the transmission of the infection by flies fed on diseased birds. The period of incubation is long (34 to 38 days). The earliest forms in the blood of the bird measure 1-2 μ in diameter. After three or four days they attain a length of 8 μ and begin to show hæmozoin granules in their cytoplasm.

H. passeris (var. A.) (Celli and Sanfelice, 1891). In *Passer italiæ* (Vieill.), *P. hispaniolensis* (Temm.), *P. domesticus* (L.). Sporogony unknown.

H. alaudæ (Celli and Sanfelice (var. A.), 1891). In *Alauda arvensis* (L.).

H. fringillæ (Labbé, 1894). In *Fringilla cælebs* (L.).

H. aluci (Celli and Sanfelice, 1891). In *Syrnium aluco* (L.).

H. bubonis (Celli and Sanfelice, 1891). In *Bubo bubo* (L.).

H. maccallumi (Novy and McNeal, 1904). In *Zenaidura cariolinensis*.

H. sacharovi (Novy and McNeal, 1904). In *Zenaidura cariolinensis*.

H. rouxii (Novy and McNeal, 1904). In *Passer domesticus*.

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H. majoris (Novy and McNeal, 1904). In *Merula migratoria.*

H. balfouri Sambon, 1907, in *Numida ptilorhyncha* Licht.

Other parasites probably belonging to this genus, but not named or determined, have been found in the following birds: —*Sturnus vulgaris* (L.).—*Garrulus glandarius* (L.).—*Carduelis carduelis* (L.).—*Chloris chloris* (L.).—*C. linota* (Gmel.).—*Pyrrhula pyrrhula* (L.).—*Coccothraustes coccothraustes* (L.).—*Anthus trivialis* (L.).—*Erithacus luscinia* (L.).—*Ruticilla phœnicurus* (L.).—*Pratincola rubetra* (L.).—*Anorthura troglodytes* (L.).—*Accentor collaris* (Scop.).—*Sylvia atricapilla* (L.).—*Phylloscopus bonellii* (Vieill.).—*Galerita cristata* (L.).—*Lanius excubitor* (L.).—*L. collurio* (L.).—*Merops apiaster* (L.).—*Hirundo*, spec.—*Caprimulgus*, spec.—*Asio accipitrinus* (Pall.).—*Tinnunculus tinnunculus* (L.).—*Accipiter nisus* (L.).—*Turtur turtur* (L.).—"Poule de Carthage."—*Melospiza fasciata* (Gmel.).—*Bubo virginianus* (Gm.).—*Melospiza georgiana* (Lath.).—*Agelaius phœniceus* (L.).—*Padda oryzivora* (L.).

To this genus probably belong the following parasites of Reptiles:—

H. testudinis (Laveran, 1905) (= *Hæmamœba testudinis*)

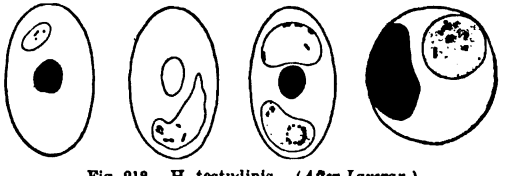

Fig. 213.—H. testudinis. (*After Laveran.*)

(Fig. 213.) In blood of *Testudo pardalis*, S. Africa. Sporonts 20 μ long by 7-8 μ broad. Schizogony not observed. Sporogony unknown.

H. metchnikovi Simond (= *Hæmamœba metchnikovi*) (Fig.

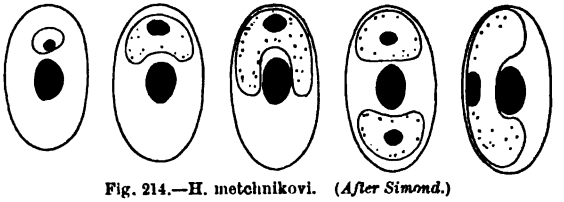

Fig. 214.—H. metchnikovi. (*After Simond.*)

214). In a water tortoise, *Trionyx indicus*. Sporonts ♂ 6-10 μ ♀ 9-10 μ. Host cell unaltered. Schizogony not observed. Sporogony unknown.

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B. TRYPANOSOMINÆ. SAMBON, 1906.

Schizont alternately free in plasma and epi- or endocellular (erythrocytes, tissue cells); no hæmozoin; free forms flagellate; resting forms rounded and without locomotor apparatus. *Schizogony* by longitudinal binary division or by multiple segmentation (rosette formation) both in free and resting forms. *Sporonts* free, and similar in structure to schizonts. *Sporogony* in Insecta, Ixodidæ, and Hirudinea.

Four Genera:

(1) *Babesia.*
(2) *Leishmania.*
(3) *Trypanosoma.*
(4) *Trypanoplasma.*

(1) Babesia. Starcovici, 1893.

One genus.

Synonyms. — *Hæmatococcus* Babes, 1888; *Pyrosoma* Smith and Kilborne, 1893; *Ixodioplasma* Schmidt, 1904; *Apiosoma* von Wandollek, 1895; *Piroplasma* Patton, 1895.

Schizont alternately free in plasma and epi- or endocorpuscular (in erythrocytes). Free form provided with flagellum

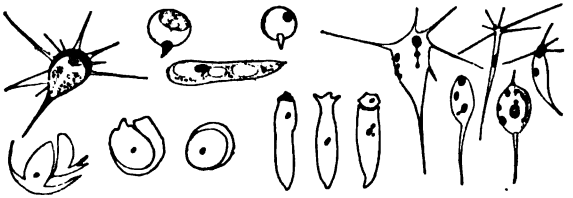

Fig. 215.—Developmental forms of Babesia canis in tick's gut. (*After Koch, Klein and Christophers.*)

which may terminate either in a point or in one or more minute rounded knobs. Epi- or endocellular form actively amœboid, presents nucleus including blepharoplast. In its earlier stage it appears ring-shaped. *Schizogony* by a process of budding which gives rise to a number of round merozoites. *Sporonts* endoglobular, pear-shaped, provided with nucleus and blepharoplast. They multiply asexually within the blood by longitudinal fission (cf. Hæmogregarina, Trypanosomia) and become sexually differentiated. According to Kinoshita the sporonts grow more slowly, are less amœboid, and preserve from the first their pyriform shape. The dividing forms may remain long connected at their pointed ends by a delicate filament, and further division may take place whilst they are still coherent, giving rise to cross forms or to rosette forms of as many as sixteen bodies. *In vitro* the microgametocytes may extrude a long pseudopodium-like filament which contains chromatin and is probably a microgamete.

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Sporogony in Ixodidæ. Within the stomach of the engorged female ticks, according to Koch and Klein, the sporonts become free and aggregate in clusters, projecting numerous fine protoplasmic processes from their broadest end; the macrogametes assume a globular shape, whilst the microgametocytes become wedge-shaped and apply themselves round the former. The oökinete is club-shaped and closely resembles the oökinetes of Plasmodium and Hæmoproteus. In the eggs of infected ticks Koch found large pear-shaped forms about four times the size of the sporont as seen in the vertebrate's blood. Quite recently Miyajima succeeded in cultivating *B. parva* from Japanese oxen in ordinary bouillon and saw the oökinetes develop into flagellated organisms similar to the culture forms of typical trypanosomes. Already in 1904 Schaudinn had suggested that the Babesiæ might be allied to the trypanosomes, basing his suggestion on the discovery of trypanosome-like forms by Kossel and Weber in the blood of Finnish oxen suffering from hæmoglobinuric fever and in smears from the contents of the intestine of ticks fed on infected animals.

Type species *B. bigemina.*

SPECIES DETERMINED:

B. bigemina (Smith and Kilborne, 1893) (= *Pyrosoma bigeminum* Smith and Kilborne, *Apiosoma bigeminum* Wandollek, *Piroplasma bigeminum* Patton, *Babesia boris* Chauvelot c.p., *Ixodioplasma specificum bovum* Schmidt). Cause of Texas fever in oxen. Sporonts 1 to 3 μ in length. Sporogony in *Margaropus australis* (Fuller) in S. America, Cuba, Porto Rico, Australia, Philippine Islands. *M. decoloratus* (Koch) S. Africa.

B. bovis (Babes, 1888) (= *Hæmatococcus bovis* Babes, *Piroplasma bigeminum* Auct. c.p.). Cause of hæmoglobinuric fever "red water" in European oxen and in "red deer," *Cervus elaphus* L. Sporogony in *Ixodes reduvius* L., *Margaropus annulatus* (Say.).

B. parva (Theiler) (=*Piroplasma parvum* Theiler). In oxen.

Fig. 216.—Babesia parva. (*After Theiler.*)

Morphologically its minute size and the frequent occurrence of rod-shaped forms separate this parasite from *B. bovis.* Moreover it cannot be communicated by blood inoculation. Sporogony in *Rhipicephalus appendiculatus* Neum, *R. simus* Koch. (Fig. 216)

B. mutans (Theiler, 1907) (= *Piroplasma mutans* Theiler). In oxen. Sporogony unknown.

B. cervi França and Borges 1907. In the blood of fallow

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deer, *Cervus dama* L. Sporonts 1 to 1·5 μ long by 0·75-1 μ broad. Sporogony unknown.

B. ovis (Babes) (= *Hæmatococcus ovis* Babes, *Piroplasma ovis* Laveran, *Amœbosporidium polyphagum* Bonome). In blood of sheep. Causes disease called "Carceaz" in Roumania. Sporogony in *Rhipicephalus bursa* Can and Fanz.

B. equi (Laveran) (= *Piroplasma equi* Lav.). In the blood of horses in S. Africa and Madagascar. Sporogony in *Rhipicephalus evertsi* Neum.

To the above species are ascribed similar parasites found in the blood of the mule and donkey and, according to Koch, by Kudicke in the zebra.

B. canis (Piana and Galli-Valerio) (= *Piroplasma bigeminum* var. *canis* Piana and Galli-Val., *Piroplasma canis* Laveran).

Fig. 216A.—Schizogonic cycle of Babesia canis. (*After Nuttall.*)

Causes "malignant jaundice" in dogs. Sporonts 5 to 6·5 μ long by 2·5 to 3·5 μ broad. Sporogony in *Hæmaphysalis leachi* Andouin in S. Africa, *Dermacentor reticulatus* (Fabr.) in Europe. Christophers claims to have worked out the sporogony of this Babesia in *Rhipicephalus sanguineus* (Latrulle). He says the oökinete gives rise to an oöcyst which may attain a diameter of 25 μ, then it breaks up into sporoblasts which may separate, and in turn give rise to sporozoites. In nymphal ticks the development takes place in the protoplasm of the embryonic tissue cells, which are already beginning to shape the future adult. In adult ticks the oökinete migrates to the ovaries, and infection is transmitted hereditarily. (Figs. 216, 216A.)

B. vesperugina (Dionisi, 1898) (= *Achromaticus vesperuginis* Dionisi). In the noctule, *Vesperugo noctula* Schreber. Sporonts 2 to 3 μ long by 0·3 to 1 μ broad; sexual differentiation marked. Sporogony unknown, possibly in *Hæmalastor vespertilionis*.

B. rossi Sambon, 1907. Found by Philip H. Ross in monkeys (*cercopithecus*) at Kikuyu, E. Africa. Pear-shaped sporonts 2·5 μ by 1·5 μ; double form very rare. Invertebrate host unknown.

Other babesiæ have been mentioned as occurring in monkeys and in goats in Africa. In 1902 Wilson and Chowning announced the discovery of a babesia in patients suffering from "spotted fever" in the Rocky Mountains, and proposed to name the new parasite *Piroplasma hominis*. At about the same time, Gotschlich, in Egypt, stated that he had found a babesia in patients suffering from typhus fever. These findings have not been confirmed. Sambon suggests that blackwater fever may be due to a minute babesia.

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(2) LEISHMANIA. ROSS, 1903.

Synonyms. — *Piroplasma* Laveran and Mesnil, 1903, *pro parte; Herpetomonas* Rogers, 1904, *pro parte; Helcosoma* Wright 1903.

Schizogonic cycle very imperfectly understood. Round, oval or oat-shaped bodies, with nucleus and blepharoplast, are found in leucocytes, in endothelial cells and in other undetermined elements. They are very numerous in the internal organs (spleen, liver, kidneys, mesenteric glands, bone marrow), and multiply by longitudinal division. Some forms (males?) segment into about eight small forms. In 1904 Rogers succeeded in cultivating these parasites in citrated blood, kept in a cold incubator at 27° C., and found that they enlarge very rapidly, assume an elongated pyriform shape and become flagellated. The flagellum arises from the blepharoplast, and projects at once clear of the body as in culture forms of typical trypanosomes. *Sporogony* unknown. Probably in insects.

Type species *Leishmania donovani*.

SPECIES DETERMINED:

L. donovani Ross, 1903 (= *Piroplasma donovani* Laveran

Fig. 217.—Leishmania donovani. (*After Leishman.*)

and Mesnil, 1903; *Herpetomonas donovani* Rogers, 1904). Cause of Kala-azar. Sporonts 2 to 4 μ in diameter. Sporogony according to Patton in *Cimex macrocephalus* Fieb.

L. tropica (Wright, 1903) (= *Helcosoma tropicum* Wright). Cause of Oriental sore (Delhi sore). Morphologically indistinguishable from *L. donovani*. Sporogony unknown.

(3) TRYPANOSOMA. GRUBY, 1843.

Synonyms. — *Amœba* Gulge, 1842; *Paramœcium* Gulge, 1842; *Undulina* Lankester, 1871; *Herpetomonas* Kent, 1878; *Hæmatomonas* Mitrophan, 1883; *Trypanomonas* Danilewsky, 1885; *Trypanozoön* Lühe, 1906.

Schizont alternately free in plasma and epi- or endocellular. Flagellum of free form in peripheral circulation bent backwards and attached along dorsal ridge of body by a thin membrane (undulating membrane), remaining portion free beyond posterior extremity of body. Resting form becomes rounded, casts off locomotor apparatus, but retains two chromatine masses (nucleus and blepharoplast). *Schizogony* by rapid longitudinal fission and by unequal or equal multiple division. *Sporogony* in Insecta and Hirudinea.

Type species *T. Lewisi*.

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SPECIES DETERMINED :

TRYPANOSOMES OF MAMMALS.

T. lewisi (Kent, 1879) (= *Herpetomonas lewisi*, Kent. *Trichomonas lewisi* Crookshank, 1886; *Trypanomonas lewisi*, Labbé, 1891; *Trypanosoma sanguinis* Kanthak, Durham and Blandford, 1898; *Trypanosoma rattorum*, Börner, 1901; *Trypanomonas murium*, Danil., 1899). (Fig. 218.) In *Mus norvegicus* Erxl. (= *Mus decumanus*, Pall.), *M. rattus*, L. and *M. rufescens* Gray. Average size, 24 to 25 μ by $1\frac{1}{2}$ to $1\frac{3}{4}$ μ. Sporogony, according to Prowazek, in the rat-louse, *Hæmatopinus spinulosus*. Fleas may also serve the purpose of transmission.

T. cricetí Lühe, 1906 (= *T. rabinowitschi* Brumpt). In hamster, *Cricetus cricetus* (L.).

T. cuniculi R. Blanchard, 1906. In rabbit, *Lepus cuniculus* L.

T. duttoni Thiroux, 1905. In mouse, *Mus musculus* L., at Saint Louis (Senegal). 25 to 30 μ long by 2·5 μ broad. Free portion of flagellum 6·5 to 10 μ long. Definitive host unknown.

Fig. 218. — T. lewisi. (*After Laveran.*)

Fig. 219.—T. gambiense.

Fig. 220. — T. brucei. (*After Laveran.*)

T. indicum Lühe, 1906. In palm squirrel, *Funambulus palmarum* (L.), at Madras. 18 to 20 μ. Definitive host unknown.

T. blanchardi Brumpt, 1905. In fat dormouse, *Myoxus glis* (L.).

T. myoxi R. Blanchard, 1906. In common dormouse, *Muscardinus avellanarius* (L.). About 20 μ long.

T. pestanai Bettencourt and França, 1905. In the common badger, *Meles taxus* (Schreb.). 30 to 32 μ by 5 to 6·5 μ. Free portion of flagellum 4·5 to 5 μ long.

T. vespertilionis Battaglia, 1905. In the noctule, *Vespertilio noctula* L. 12 to 15 μ long by 2 to 3 μ broad.

T. nicolleorum Sergent, Ed. and Et., 1905. In *Myotis myotis*, (Bechst.), and in *Vespertilio kuhli* Natt. In Algeria and Tunis. 20 μ to 24 μ by 1·5 μ. Free portion of flagellum 4 to 5 μ.

T. dionisii Bettencourt and França, 1905. In *Vesperugo pipistrellus*, *V. serotinus*, and *V. nattereri*. Portugal

Other species have been reported for *Miniopterus schreibersii* in Italy, *Pteropus medius* in Madras, *Pipistrellus pipistrellus* in England, but they have not been described and are as yet unnamed. Durham found a trypanosome in the stomach of a *Stegomyia fasciata* in blood which it had imbibed from a bat (*Phyllostoma* spec.).

T. gambiense Dutton, 1902 (Fig. 219) (= *T. nepveui* Sambon, 1903; *T. hominis* Manson, 1903; *T. castellanii* Kruse, 1903; *T. fordii* Maxwell, Adams, 1903; *T. ugandense* Castellani, 1903).

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Cause of sleeping sickness. In Man. 17 to 28 μ long by 1·4 to 2 μ broad. Sporogony in *Glossina palpalis*. Bruce, Minchin, and others believe transmission by the tse-tse fly to be simply mechanical. Sambon maintains that the insect acts as a true alternative host, and that the infection may be transmitted hereditarily.

T. evansi (Steel, 1885) (= *Spirochæta evansi* Steel. *Hæmatomonas evansi* and *Trichomonas evansi* Crookshank, 1886). 25 μ long by 1·5 μ broad. Cause of surra disease in horses in India. Recently imported into Mauritius and the Philippines. Probably transmitted by a stomoxys or a tabanus. In Mauritius the epidemic is thought to have been spread by *Stomoxys nigra*.

T. brucei Plimmer and Bradford, 1899. (Fig. 220.) Average size 28 to 30 μ by 1·5 to 2·5 μ. Cause of nagana disease in horses, cattle and other animals in South and South-east Africa. Sporogony in various species of Glossina.

T. equiperdum Doflein, 1901 (= *T. rougeti* Lav. and Mes.). 25 to 28 μ by 1·5 to 2 μ. Cause of dourine in Algeria and in certain parts of Southern Europe. Transmission as a rule in a direct manner during the act of coïtus. Possibly in some cases through the agency of an insect host.

T. equinum Voges emend, 1902 (= *T. elmassiani* Lignières). (Fig. 221.) 22 to 25 μ by 1·5 to 2 μ. Blepharoplast exceedingly minute. Cause of Mal de Caderas in horses in Argentina and Central South America. Usual intermediary host probably *Hydrochærus capybara*. Transmitting agent a tabanus or stomoxys.

Fig. 221. — T. equinum. (*After Laveran.*)

Fig. 222. — T. theileri. (*After Laveran.*)

Fig. 223.—T. avium. (*After Laveran.*)

T. dimorphon Laveran and Mesnil, 1904. In horses in Senegambia. Transmitting agent, possibly, *Glossina palpalis*.

T. theileri Laveran, 1902 (= *T. transvaaliense* Laveran, 1902). Medium size 50 μ long by 3·5 to 4 μ broad. Cause of "Galziekte" or bile-sickness in cattle in the Transvaal. (Fig. 222.)

T. nanum Laveran, 1905. 10 to 14 μ in length by ·5 to 2 μ in breadth. No free flagellum or extremely short. Undulating membrane poorly developed. Blepharoplast large. Found by Balfour in cattle in the Anglo-Egyptian Soudan.

T. pecaudi Laveran, 1906. In horses and cattle of Soudan. Long slender form 25-35 μ long by 1·5 μ wide; short, stumpy form, 14-20 μ long by 3-4 μ wide.

T. vivax Ziemann, 1905. In sheep, goats and cattle in the Cameroons, 18 to 26 μ in length by 2 to 2·5 μ in breadth.

T. cazalboui Laveran 1906. In horses and cattle of French Soudan. Transmitting agent, according to Cazalboui, *Tabanus niger*.

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T. congolense Broden, 1904. In sheep of the Congo Free State. Length 10·5 to 15·5 μ, breadth 1·7 to 2·5 μ.

T. suis Ochmann, 1905. In pigs of German East Africa.

TRYPANOSOMES OF BIRDS.

T. avium Laveran, 1903. (Fig. 223.) In the wood-owl, *Syrnium aluco* (L.). Length 35 to 45 μ, inclusive of flagellum.

T. confusum Lühe, 1906 (= *T. avium* Novy and McNeal, 1904). Two forms, one more common, 20 μ by 3 to 5 μ, free portion of flagellum 10 μ in addition; the other less frequent, 50 by 6 μ, free portion of flagellum 15 to 20 μ extra. In the following North American birds: *Agelaius phœniceus* (L.), *Sialia sialis* (L.), *Cyanocitta cristata* (L.), "*Icterus galbula*," *Merula migratoria* (L.), *Passer domesticus* (L.), and *Melospiza fasciata* (Gmel.).

T. laverani Novy and McNeal, 1905. In *Astragalinus tristis* (L.). North America.

T. mesnili Novy and McNeal, 1905. In the lineated buzzard. *Buteo lineatus* Vieill. North America. Length 50 μ; breadth 8.

T. paddæ Laveran and Mesnil, 1904. In the Java sparrow, *Padda oryzivora* (L.). 30 to 40 μ long by 5 to 7 μ broad.

T. johnstoni Dutton and Todd, 1903. In *Estrelda astrild* (L.). Senegambia. 36 to 38 μ long by 1·4 to 1·6 μ broad. Undulating membrane narrow and poorly developed. No free portion of flagellum.

T. mathisi Ed. and Et. Sergent, 1907. In blood of swallow. 22 μ long by 4 μ broad. Undulating membrane well developed.

T. polyplectrum Vassal, 1905. In *Polyplectrum germani*, a pheasant in Annam. Length 46 μ; breadth 5 μ. Free portion of flagellum 12 μ long.

Danilewsky records finding Trypanosomes in owls and in the European roller, *Coracias garrula*, L., Hanna in crows and pigeons in India, the brothers Sergent in various Algerian birds, *e.g.* in *Carduelis carduelis* (L.), *Sylvia atricapilla* (L.) and *Hirundo* spec., Donovan in *Athene brama* (Temm.), the spotted owl, Madras, and in the Indian kite, *Milvus govinda* Sykes; Ziemann in the common chaffinch, *Fringilla cœlebs*, L.; Neave in the Egyptian vulture, *Neophron percnopterus* (L.), and the red-breasted shrike, *Laniarius cruentus*, in the Soudan; Dutton, Todd and Tobey in the trumpeter hornbill, *Bycanistes buccinator*, and other birds.

Fig. 224.—T. damoniæ. (*After Laveran and Mesnil.*)

TRYPANOSOMES OF REPTILES.

T. damoniæ Laveran and Mesnil, 1902. (Fig. 224.) In tortoise *Damonia reevesi* (Gray). Length 32 μ, breadth 4 μ.

Trypanosomes have been observed by Simond in *Kachuga tectum* (Gray), by Dutton and Todd in tortoises, crocodiles and snakes in S. Africa, and by Gehrke in a gecko.

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TRYPANOSOMES OF AMPHIBIA.

T. rotatorium (Mayer) (Fig. 225) (= *Amœba rotatoria* and *Paramœcium loricatum* sive *costatum* Mayer, July, 1843; *Trypanosoma sanguinis* Gruby, November, 1843; *Monas rotatoria* Lieberk, 1870; *Undulina ranarum* Lankester, 1871; *Paramœcioides costatus* Grassi, 1882). In *Rana esculenta*, L. Length

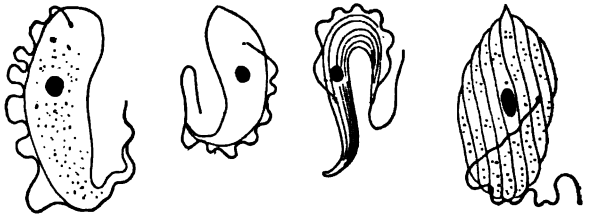

Fig. 225.—T. rotatorum. (*After Laveran.*)

40 to 60 μ, breadth 5 to 40 μ. Undulating membrane well developed and thrown into numerous folds. Two principal types, one with smooth regular surface, the other with surface thrown into parallel ridges running either longitudinally or spirally. Sporogony probably in a leech.

To the above species have been ascribed similar parasites found in *R. temporaria* L., *R. trinodis* (?), *R. galamensis*, D. and B., *R. oxyrhynchus* Sund.; *R. mascarensis*, B., *R. marmorata* Rapp., *Hyla arborea* L., *Bufo viridis* Laur., *B. regularia* Renn. For toads, Durham believes that a tick may be the transmitting agent.

Fig. 226.—T. mega.

T. boueti Martin, 1907. In *Mabuia raddonii*. Somewhat similar in shape to *T. rotatorium*. Length 40 μ; breadth 40 μ. No free portion to flagellum. Nucleus crescent shaped.

T. mega Dutton and Todd, 1903 (Fig. 226) (=*T. Karyozenkton* Dutton and Todd, 1903). In *Rana* spec. 82 to 87 μ long by 8 μ maximum breadth. Free portion of flagellum 10 to 15 μ long. Anterior portion of body smooth, posterior two-thirds presenting longitudinal ridges and furrows, which give the appearance of alternating darker and lighter bands.

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T. inopinatum Ed. and Et. Sergent, 1904 (Fig. 227); 25 to 30 μ long, 3 μ broad. In *Rana esculenta* L. Sporogony, according to Billet, in a leech. *Helobdella algira* Moqu-Tand. Brumpt confirmed Billet's researches and showed that *T. inopinatum* when taken up by the leech rapidly assumes the herpetomonad form, and that infested leeches when placed on a "clean" frog, even as late as a month after the first feeding, produce a severe and even fatal trypanosomal infection after a period of incubation of from eight to ten days. Billet regards this trypanosome as related to *Hæmogregarina minima*. (*See* p. 822.)

T. nelspruitense Laveran, 1904. In *Rana* spec. in the Transvaal; 24 to 35 μ long by 2·5 to 3·5 μ broad. Free portion of flagellum extremely long (25 μ or more), almost as long as the body.

T. somalense Brumpt, 1906. In a toad of Somaliland, *Bufo reticulatus*. Length, 39 μ. Free portion of flagellum 7 μ. Nucleus in anterior end close to blepharoplast.

T. borrelli Marchoux and Salimbeni, 1907. In a tree frog

Fig. 227.—T. inopinatum.

Fig. 228.—T. remaki.

closely allied to *Hyla lateristriga* Brazil. Similar in shape to *T. rotatorium*. Diameter, 80 μ. No free portion to flagellum.

TRYPANOSOMES OF FISHES.

T. remaki Laveran and Mesnil, 1901 (Fig. 228). In pike, *Esox lucius* L. Body slender, nucleus in posterior half. Two forms described probably representing sexual differentiation. Var. *parva*, 30 to 42 μ long by 1·5 μ broad. Free portion of flagellum 10 to 12 μ long. Cytoplasm faintly staining. Var. *magna*, 45 to 57 μ long by 2 to 2·5 μ broad. Free portion of flagellum 17 to 20 μ long. Cytoplasm more deeply staining.

T. danilewskyi Lav. and Mesn., 1904. In carp, *Cyprinus carpio* L. Undulating membrane better developed than in *T. remaki*, with wider folds; 35 to 45 μ long by 3 μ broad. Free portion of flagellum 15 to 17 μ long.

T. tincæ Laveran and Mesnil, 1904. In tench, *Tinca vulgaris* L.; 35 μ long by 2·5 to 3 μ broad.

T. abramis Laveran and Mesnil, 1904. In bream, *Abramis brama* L. Not described.

T. barbatulæ Léger, 1904. In loach, *Cobitis barbatula* L. Body rather stumpy, 30 to 40 μ long by 4 to 6 μ broad. Free portion of flagellum 11 to 12 μ long. Undulating membrane with large and deep folds. Sporogony in a leech, *Piscicola* spec. Eighteen hours after infection Léger observed in the leech's intestinal contents, pyriform oökinetes without flagellum;

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some of these possessed a compound nucleus, either at rest or in process of heteropolic division, while others had two nuclei, of which one was smaller than the other. Four days later, the intestine contained numerous trypanosomes, ♀ ♀ and ♂. Further evolution and manner of re-entering leech not observed.

T. cobitis (Mitrophanow emend., 1883) (= *Hæmatomonas cobitidis* Mir., *Trypanosoma piscium* and *T. fusiforme piscium*, in part, Danil.) In *Misgurnus fossilis* (L) (= *Cobitis fossilis* L.). 30 to 40 μ long by 1 to 1·5 μ broad. Free portion of flagellum 10 to 15 μ long.

T. carassii Mitrophanow, 1883. Synonyms as for *T. cobitis*. In Crucian carp, *Cyprinus carassius* L. (= *C. vulgaris* L.).

Fig. 229.—T. granulosum.

T. granulosum Laveran and Mesnil, 1902 (Fig. 229). In the eel, *Anguilla vulgaris*, Turt. Body long and narrow, 70 to 80 μ long by 2·5 to 3 μ broad. Free portion of flagellum 25 μ. Blepharoplast large. Cytoplasma filled with large deeply staining granules, which may surround and obscure the nucleus. According to Brumpt, *T. granulosum* when sucked up by a leech of the genus *Hemoclepsis* gives rise in a few hours, in the stomach, to pyriform bodies which then pass into the intestine, where they persist in the herpetomonad form for months. Such leeches when placed on "clean" eels gave a positive infection in from four to six days.

T. barbi Brumpt, 1906. In *Barbus fluviatilis*. 51 μ long by 3 μ broad. Free portion of flagellum 16 μ. Nucleus median.

T. percæ Brumpt, 1906. In the river perch, *Perca fluviatilis*. 57 μ long by 3 μ broad. Free portion of flagellum 16 μ. Nucleus median.

T. acerinæ Brumpt, 1906. In the ruff, *Acerina cernua*. 47 μ long by 3 μ broad. Free portion of flagellum 17 μ. Nucleus in posterior third.

T. phoxini Brumpt, 1906. In the minnow, *Phoxinus lævis*. 46 μ long by 5 μ broad. Free portion of flagellum 12 μ. Nucleus median.

T. langeroni Brumpt, 1906. In the Miller's thumb, *Cottus gobio*. 50 μ long by 3 μ broad. Free portion of flagellum 13 μ. Nucleus median.

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T. scardinii Brumpt, 1906. In the rudd, *Scardinius erytrophtalmus* (L.). 54 μ long by 4 μ broad. Free portion of flagellum 18 μ. Nucleus median.

T. leuciscí Brumpt, 1906. In various species of *Leuciscus*. 48 μ long by 3 μ broad. Free portion of flagellum 18 μ. Nucleus in posterior third.

T. elegans Brumpt, 1906. In the gudgeon, *Gobio fluviatilis*. 51 μ long by 4·5 μ broad. Free portion of flagellum 15 μ. Nucleus median.

T. squalii Brumpt, 1906. In the chub, *Squalius cephalus* (L.). Sporogony in stomach of *Hemiclepsis*.

T. Clariæ Montel, 1905. In *Clarias* spec. in Cochin China. Body ribbon-like; 60 μ long by 4 μ broad.

T. angolensis Sambon, 1907. Found by Dutton, Todd and Tobey in *Clarias angolensis* Steind.

T. rhamdiæ Bolelho, 1907. In *Rhamdia quelen*, a mud-fish of Brazil. Length 40 μ to 48 μ; width 2·5 μ. Undulating membrane very narrow, surrounds body spirally. No free portion of flagellum.

Fig. 230.—T. soleæ. (*After Laveran and Mesnil.*)

Fig. 231. —T. platessæ. (*After Lebailly.*)

Fig. 232.—T. flesi. (*After Lebailly.*)

Fig. 233. — T. laternæ.)

T. macrodonis Bolelho, 1907. In *Macrodon malabaricus*. Length 48 μ, width 1 μ. Undulating membrane. Very narrow. No free portion of flagellum.

Other fresh-water fish trypanosomes have been observed by Neave in the noke fish (*Mugil*), the dabib (*Polypterus*), the bagara fish (*Bagcus bayard*), and the gargur fish (*Lynodontis schal*) from the Nile.

T. soleæ Lav. and Mesn., 1901 (Fig. 230). In the sole, *Solea solea*, 1, L. (1). Length 40 μ; free portion of flagellum 8 μ. Blepharoplast spherical, very large, occupies entire width of body. Fine longitudinal striations noticeable in cytoplasm. Sporogony probably in a leech, *Hemibdella soleæ*, which was common on all the fish examined.

T. platessæ Lebailly, 1904 (Fig. 231). In the plaice, *Platessa platessa* L. 52 μ long by 3 to 3·5 μ; free portion of flagellum 12 μ. Nucleus in posterior half of body.

T. flesi Lebailly, 1904 (Fig. 232). In flounder, *Flesus flesus* L. 55 μ long by 5 μ broad; free portion of flagellum 10 μ. Nucleus median.

T. laternæ Lebailly, 1904 (Fig. 233). In *Arnoglossus laterna* (Walb) (= *Platophrys laternæ*). 65 μ long by 5 to 6 μ broad. Free portion of flagellum 8 μ.

T. bothi Lebailly, 1905 (Fig. 234). In brill, *Bothus rhombus*.

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42 μ long by 3 μ broad. Free portion of flagellum 13 μ. Nucleus in posterior half of body.

T. limandæ Brumpt and Lebailly, 1904 (Fig. 235). In *Limanda platessoides*, L. (= *L. limanda*). 45 μ long by 2 to 2·5 μ broad. Free portion of flagellum 20 μ.

Fig. 234.—T. bothi. (*After Lebailly.*)

Fig. 235.—T. limandæ. (*After Brumpt and Lebailly.*)

Fig. 236.—T. delagei. (*After Brumpt and Lebailly.*)

Fig. 237.—T. gobii.

T. delagei Brumpt and Lebailly, 1904 (Fig. 236). In shanny or smooth blenny, *Blennius pholis* L. 33 μ long by 2·5 μ broad. Free portion of flagellum 12 μ.

T. gobii Brumpt and Lebailly, 1904 (Fig. 237). In rock goby, *Gobius niger* L. 66 μ long by 5 to 5·5 μ broad. Free portion of flagellum 10 μ.

T. cotti Brumpt and Lebailly, 1904 (Fig. 238). In *Cottus bubalis* Euphr. 53 μ long by 5 μ broad. Free portion of flagellum 8 μ.

Fig. 238.—T. cotti. (*After Lebailly.*)

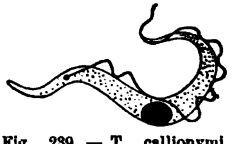

Fig. 239.—T. callionymi. (*After Brumpt and Lebailly.*)

T. callionymi Brumpt and Lebailly, 1904 (Fig. 239). In *Callionymus lyra* L. 70 μ long by 5 μ broad. Free portion of flagellum 5 to 8 μ.

T. scyllii Lav. and Mes., 1902. In dogfish, *Scyllium canicula* Cuv., and *S. stellare* L. 70 to 75 μ long by 5 to 6 μ broad. Free portion of flagellum 14 μ. Body usually rolled up on itself, often forming a complete circle. Undulating membrane with numerous well-developed folds.

T. rajæ Lav. and Mesn. (Fig. 240). In skates, *Raja*

Fig. 240.—T. rajæ. (*After Laveran and Mesnil.*)

clavata L., *R. macrorhynchus* Dum., *R. mosaica* Lacep., and *R. unctata* Risso. 75 to 80 μ long by 6 μ broad. Free portion of

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flagellum 20 μ long. Body rolled up. Sporogony probably in *Pontobdella muricata*, a leech of frequent occurrence on infected rays.

Trypanosomes have also been seen, but not described or named, in certain species of Siluridæ (*e.g. Macrones seenghala*, *M. tengara*), and in *Ophiocephalus striatus* and *Trichogaster fasciatus*.

(4) TRYPANOPLASMA. LAVERAN AND MESNIL, 1902.

Free form in peripheral blood provided with two flagella—one free at anterior extremity, the other bent backwards and attached to the body for part of its course as in Trypanosoma. Sporogony in Hirudinea.

T. borreli Laveran and Mesnil, 1902 (Fig. 241). In the rudd, *Leuciscus erythrophthalmus*, and in the minnow, *Phoxinus lævis*.

Fig. 241.—T. borreli. (*After Laveran and Mesnil.*)

20 to 22 μ long by 3·5 to 4·5 μ broad. Free flagella about equal length 13 to 15 μ long. Sporogony unknown.

T. varium Léger, 1904. In loach, *Cobitis barbatula* L. Length about 25 μ. Free flagella 18 to 20 μ. Sporogony, according to Léger, in *Hemiclepsis marginata*. Leeches placed on fish infected with *T. varium* showed in a few days numerous small, almost filiform trypanoplasmes in addition to trypanosome-like forms.

T. cyprini Plehn, 1903. In the carp, *Cyprinus carpio*. Average length 20 μ.

T. guernei Brumpt, 1905. In the Miller's thumb, *Cottus gobio* (Cuvier). 34 μ long. Free flagellum 4 μ; free portion of attached flagellum 16 μ. Blepharoplast 9 μ long; nucleus 7 μ long. Cytoplasm contains always dark granules. Sporogony in Piscicola.

T. barbi Brumpt, 1906. In blood of *Barbus fluviatilis*. 26 μ long. Free flagellum 9 μ long; free portion of attached flagellum 18 μ. Blepharoplast 11 μ long; nucleus 10 μ. Never any pigment granules in cytoplasm. Sporogony in Piscicola.

T. abramidis Brumpt, 1906. In the bream, *Abramis brama* L. 30 μ long. Free flagellum 5-6 μ long; free portion of attached flagellum 15 μ long. Sporogony in Hemiclepsis.

T. truttæ Brumpt, 1906. In the river trout, *Salmo fario* (L.). 20 μ long. Free flagellum 4 μ; free portion of attached flagellum 12 μ. Sporogony probably in Piscicola.

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